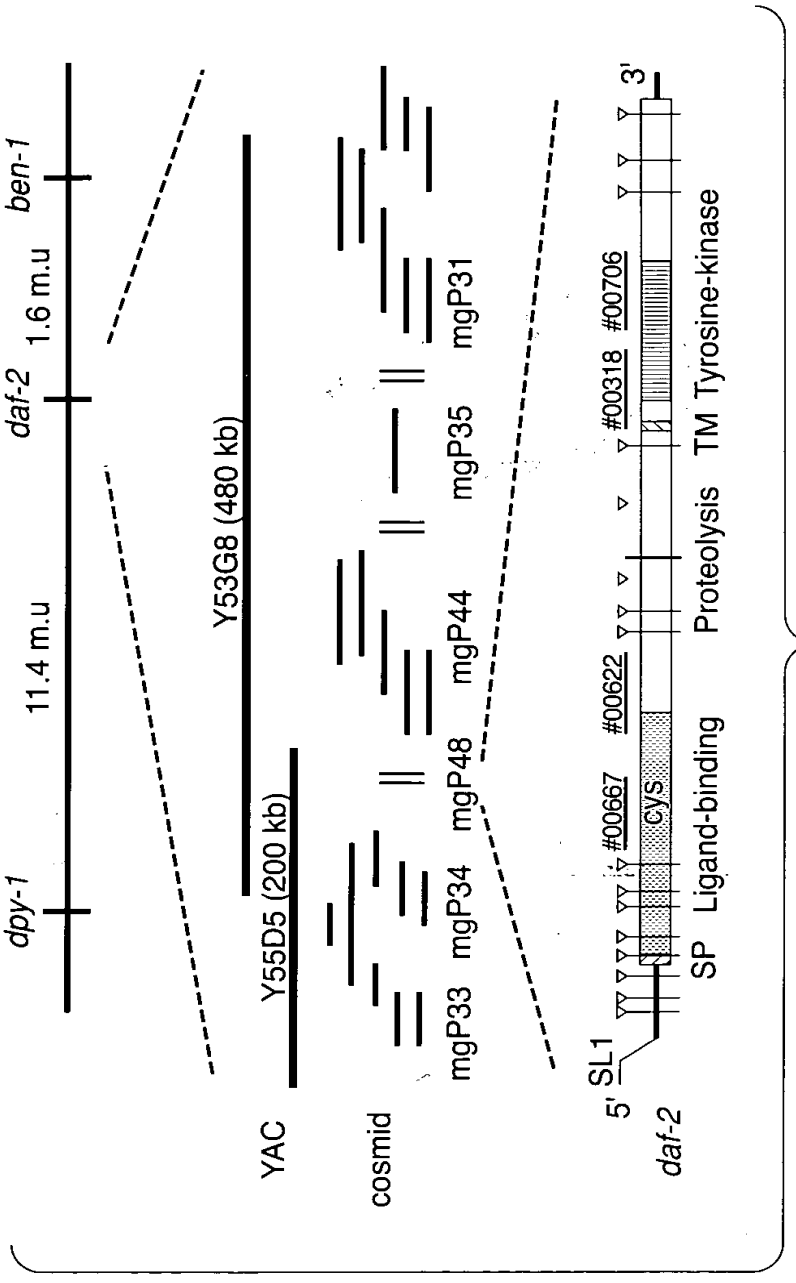

Fig. 1

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 241 SNTTCQKSCAYDRLLPTKEIGPGCDANGDRCHDQCVGGCERVNDATACHACKNVYHKGKC
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 421 HTITGYLLVRQSSPFISLNMFRNLRRIEAKSLFRNLYAITVFENPNLKKLFDSTTDLTLD
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 541 VFFSWPSFNITDIDQRKFLGYELFFKEVPRIDENMTIEEDRSACVDSWQSVFKQYYETSN
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Fig. 2A

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 151  agacgacaca aaattttgga aaatttggaa gaagagaatc tcggcccgag
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Fig. 2B (sheet 1 of 3)

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Fig. 2B (sheet 2 of 3)

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Fig. 2B (sheet 3 of 3)

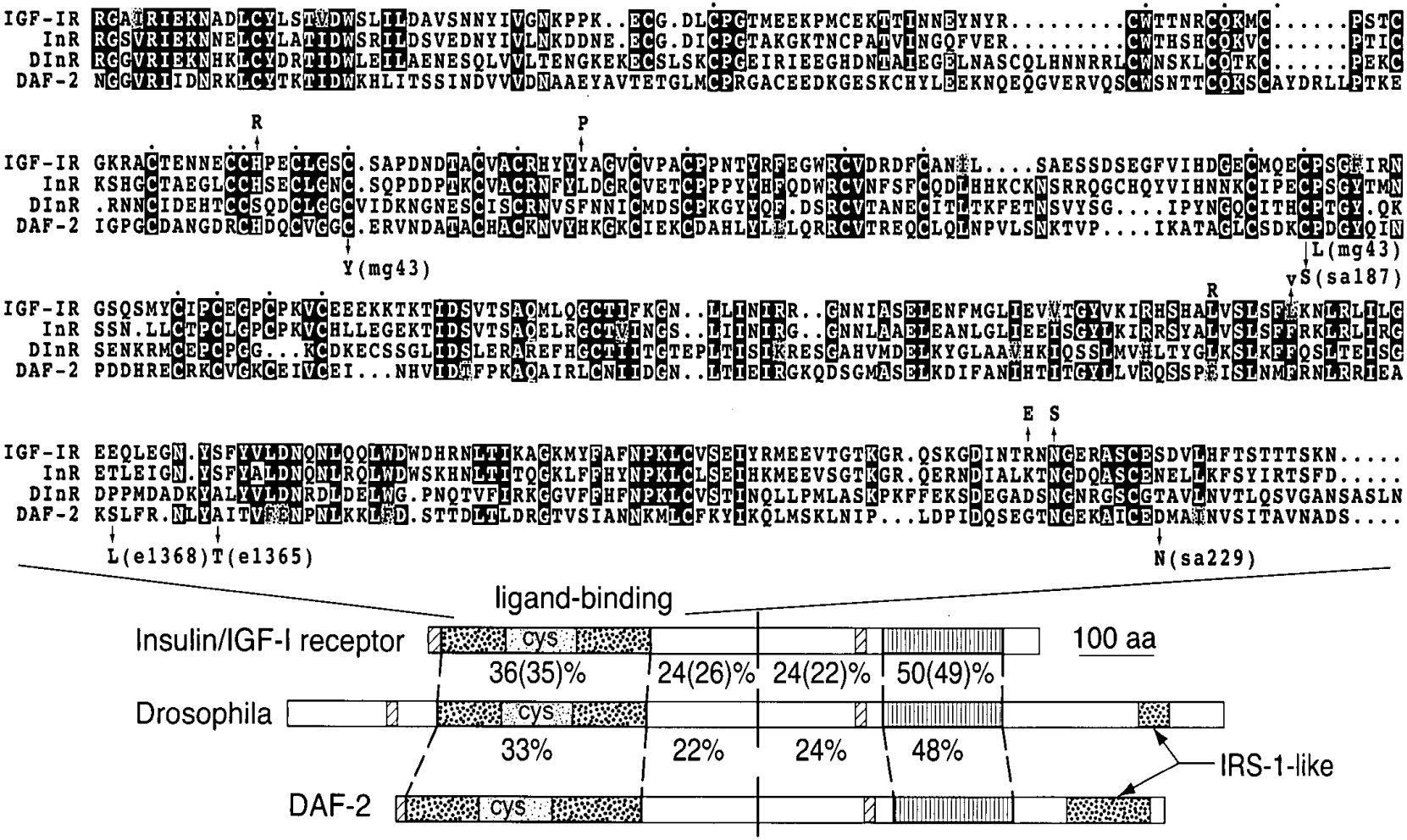


Fig. 2C (sheet 1 of 2)

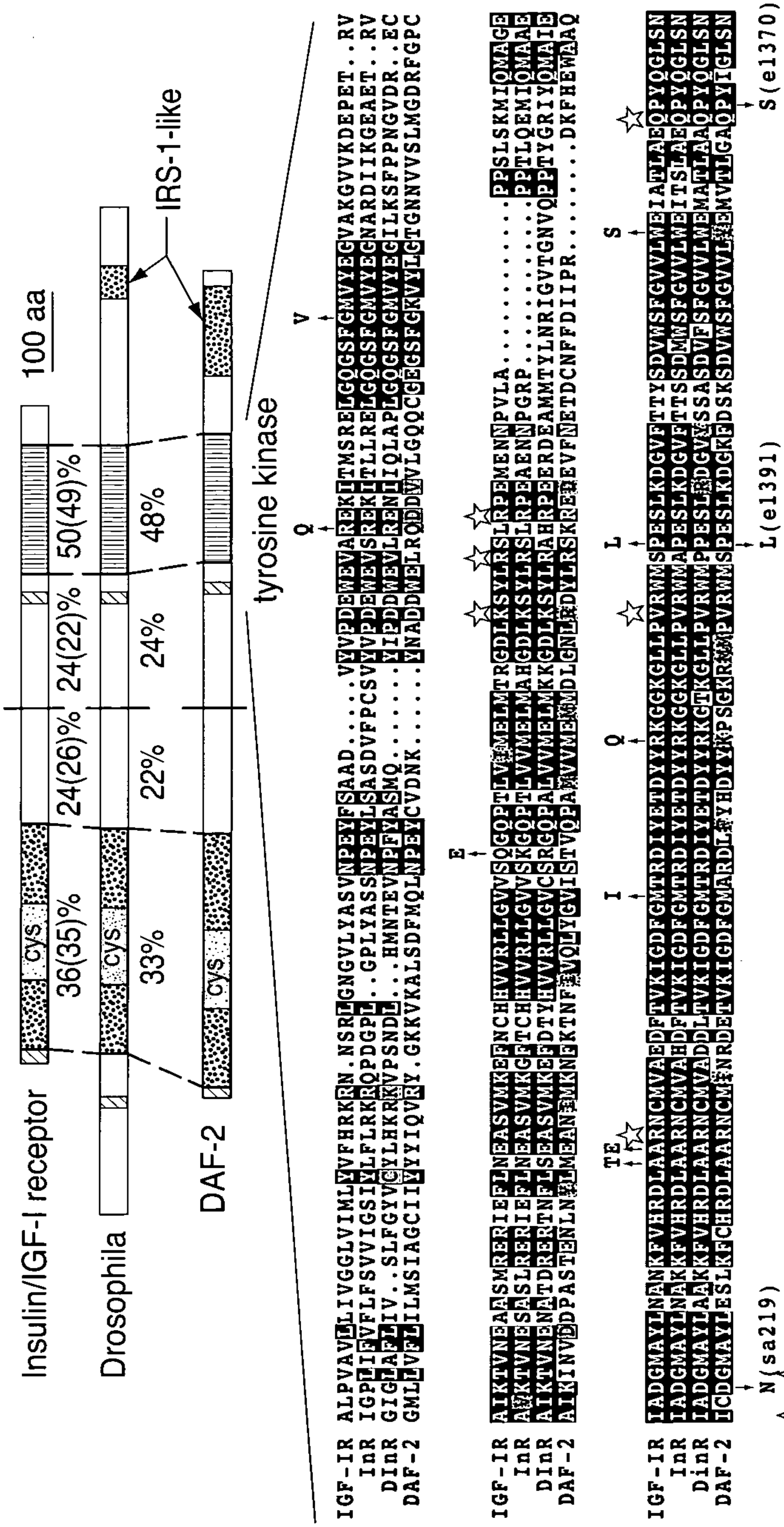


Fig. 2C (sheet 2 of 2)

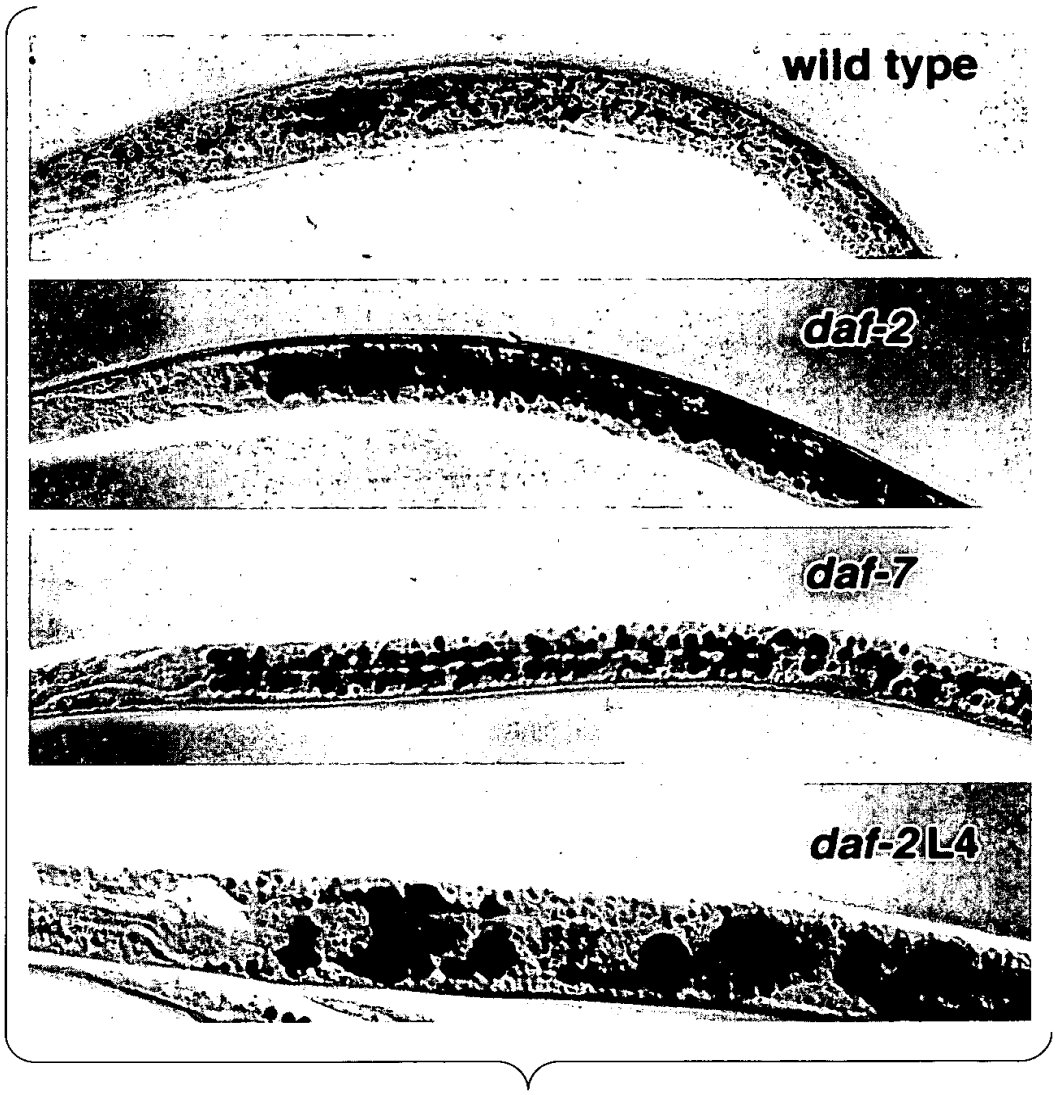
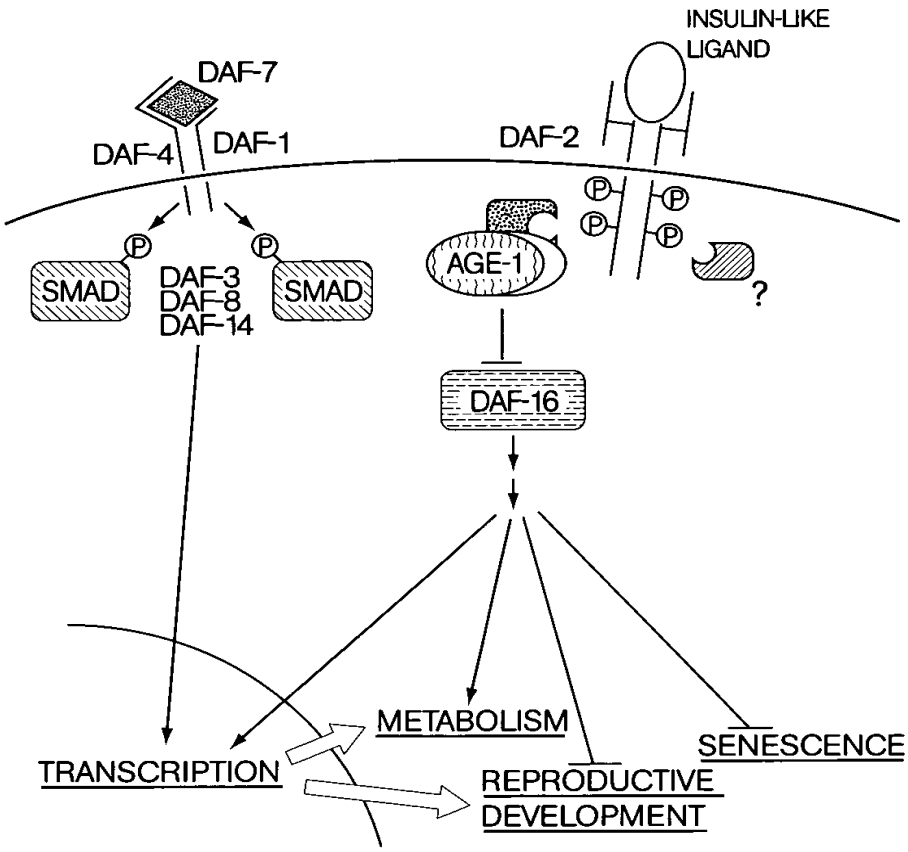


Fig. 3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LIGAND
DAF-7
DAF-4
DAF-1
DAF-2
P
SMAD
DAF-3
DAF-8
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AGE-1
?
DAF-16
METABOLISM
SENESCENCE
TRANSCRIPTION
REPRODUCTIVE
DEVELOPMENT

Fig. 4

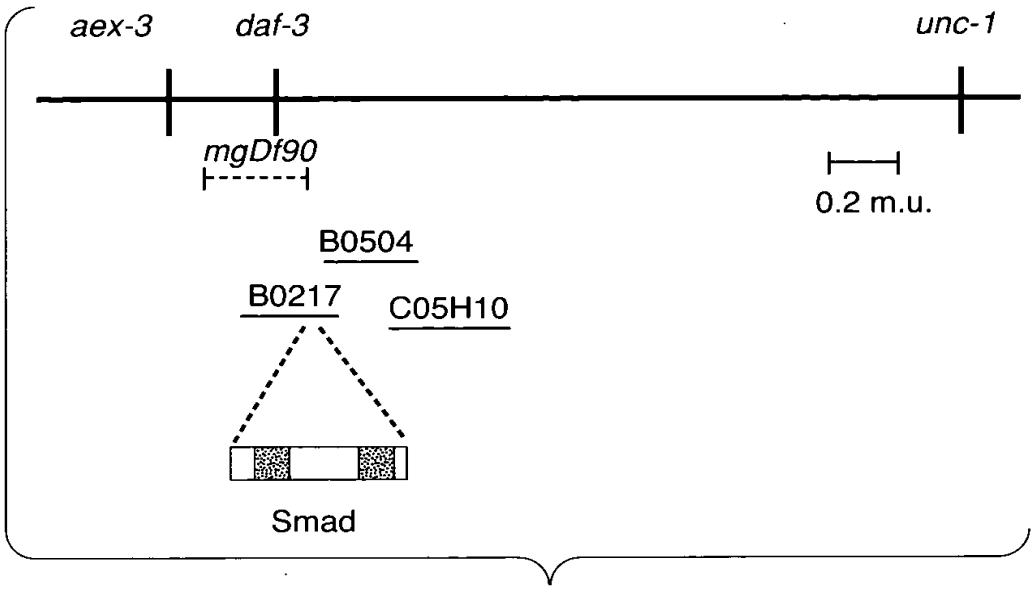
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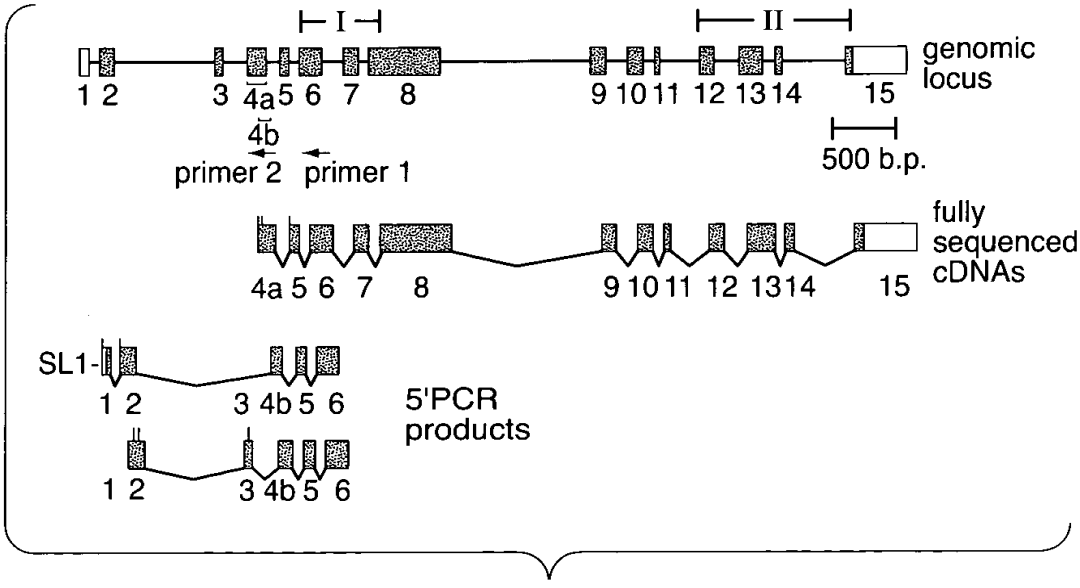
Fig. 5A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II
genomic locus
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4b
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primer 1
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SL1-
1 2 3 4b 5 6
5'PCR products
1 2 3 4b 5 6

Fig. 5B

Domain I

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             mg125 P->L
         RLQVHGRKGFPHVVYGKLWRFNEMTKNETRHVDHCKHAFEMKSDMVCVNPYH
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Domain II

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        mg132  G->E
         RKAIVDGIRFSYKKDGSVWLQNRMKYPVFVTSGYLDEQSGGLKKDKVHKVYGCA
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Fig. 5C

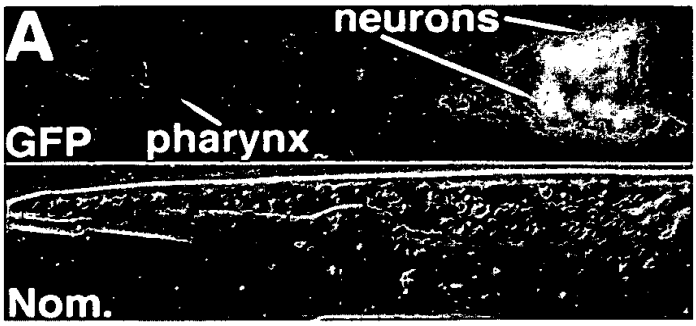


Fig. 6A

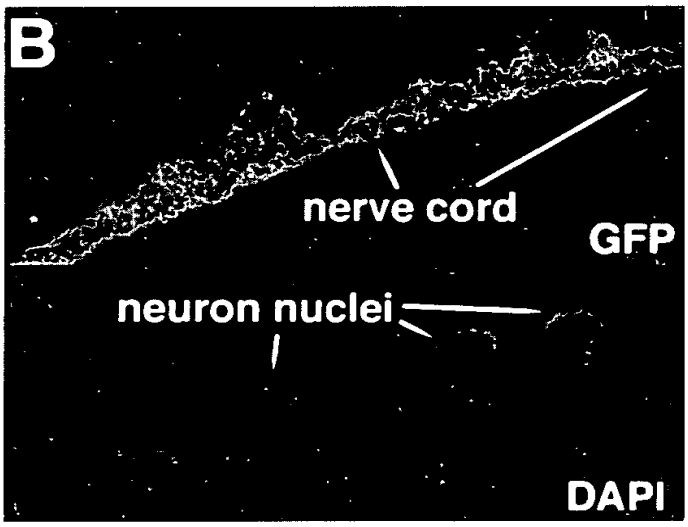


Fig. 6B

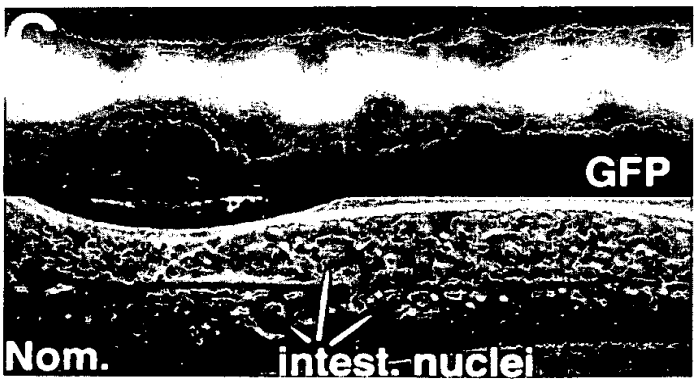


Fig. 6C

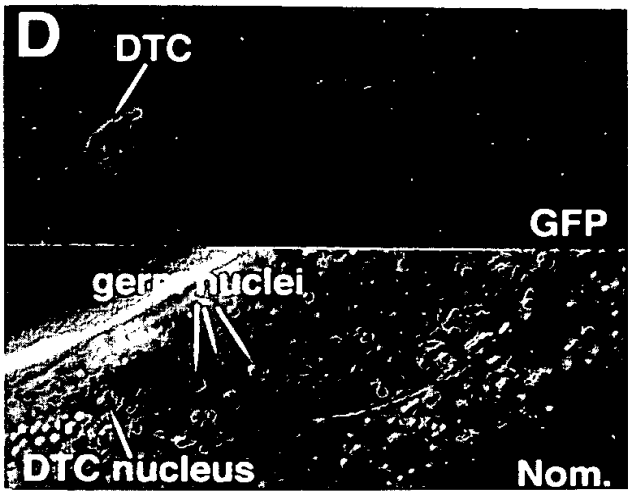


Fig. 6D

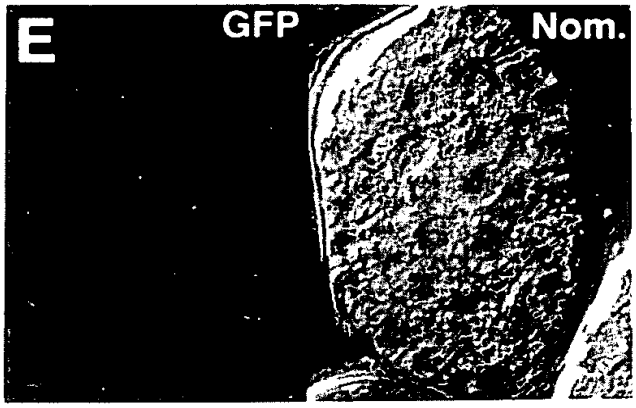


Fig. 6E

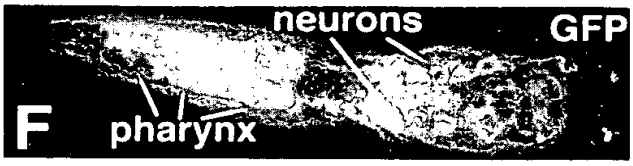


Fig. 6F

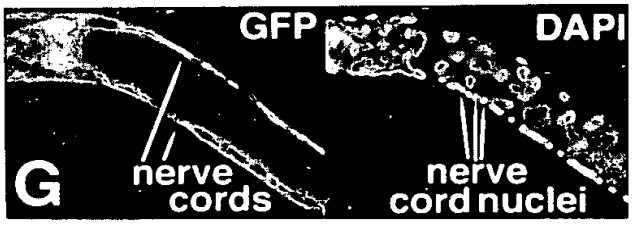


Fig. 6G

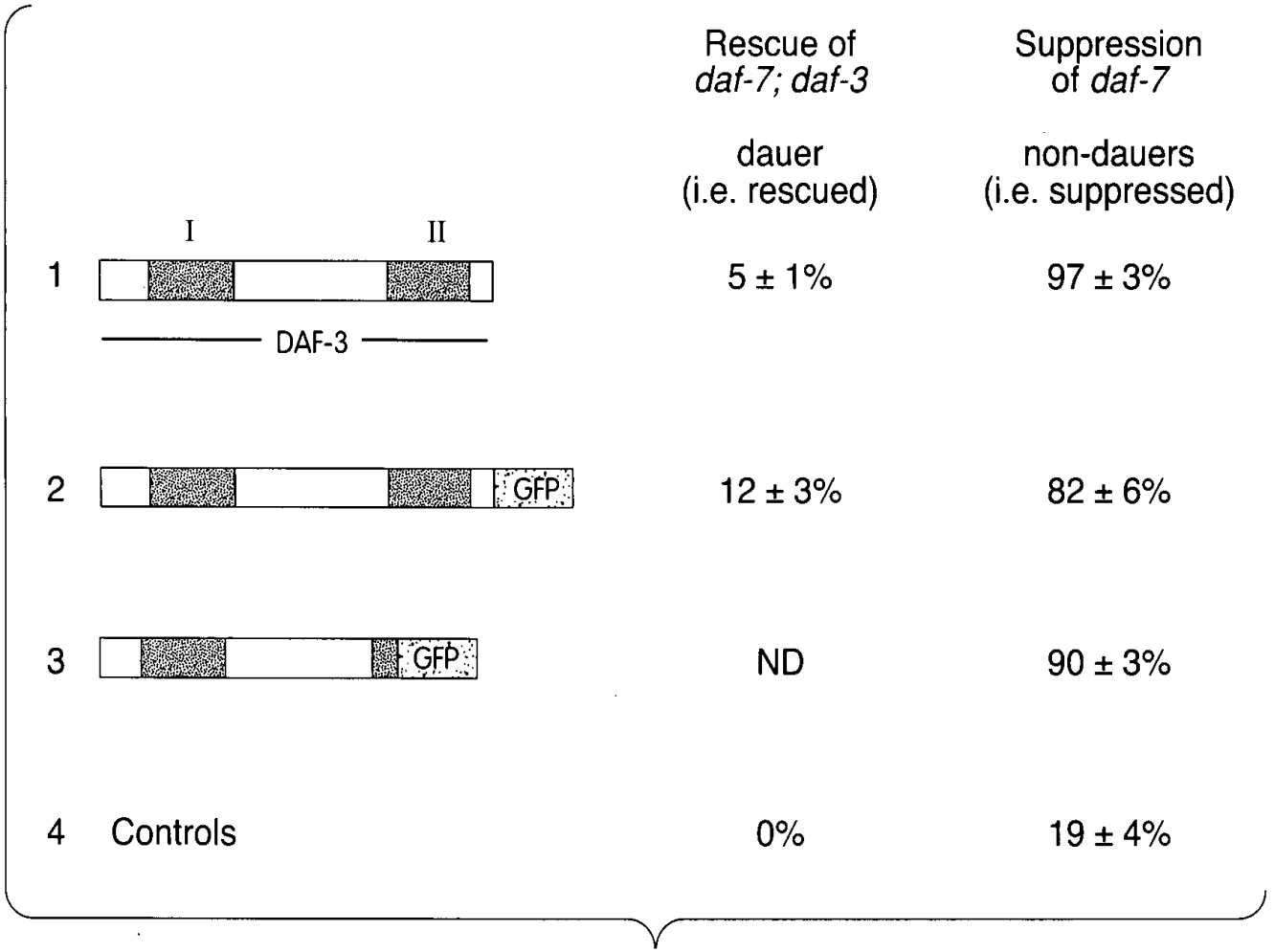
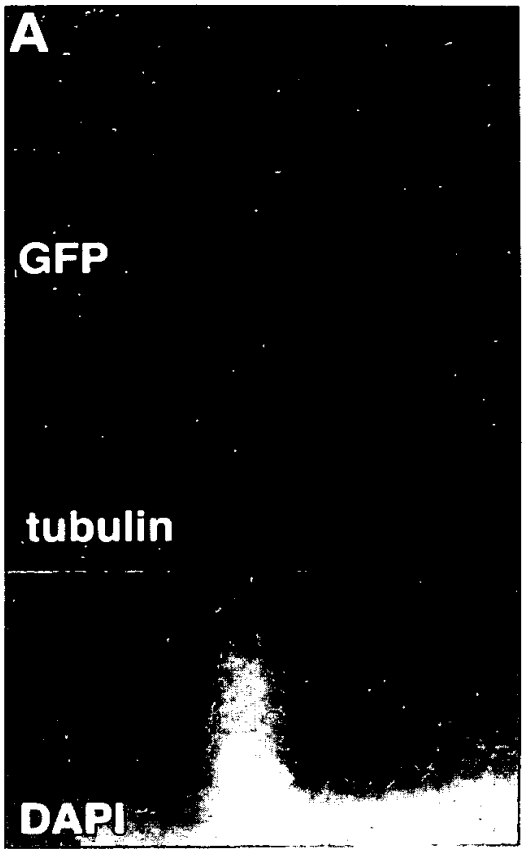

Rescue of
daf-7; daf-3
Suppression
of daf-7
dauer
(i.e. rescued)
non-dauers
(i.e. suppressed)
I
II
1
5 ± 1%
97 ± 3%
DAF-3
2
GFP
12 ± 3%
82 ± 6%
3
GFP
ND
90 ± 3%
4
Controls
0%
19 ± 4%

Fig. 7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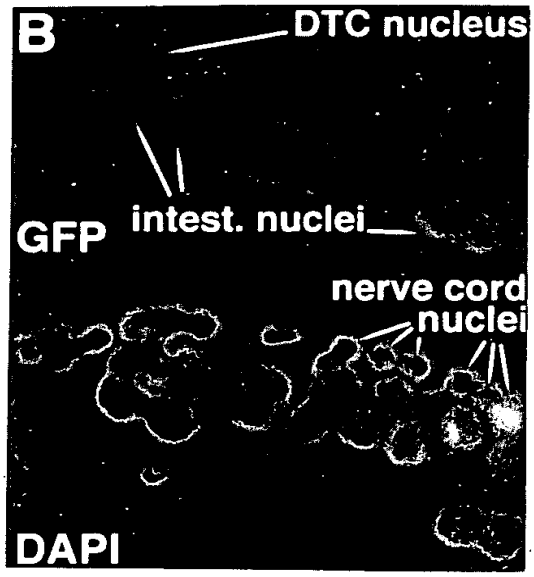
GFP
tubulin
DAPI

Fig. 8A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DTC nucleus
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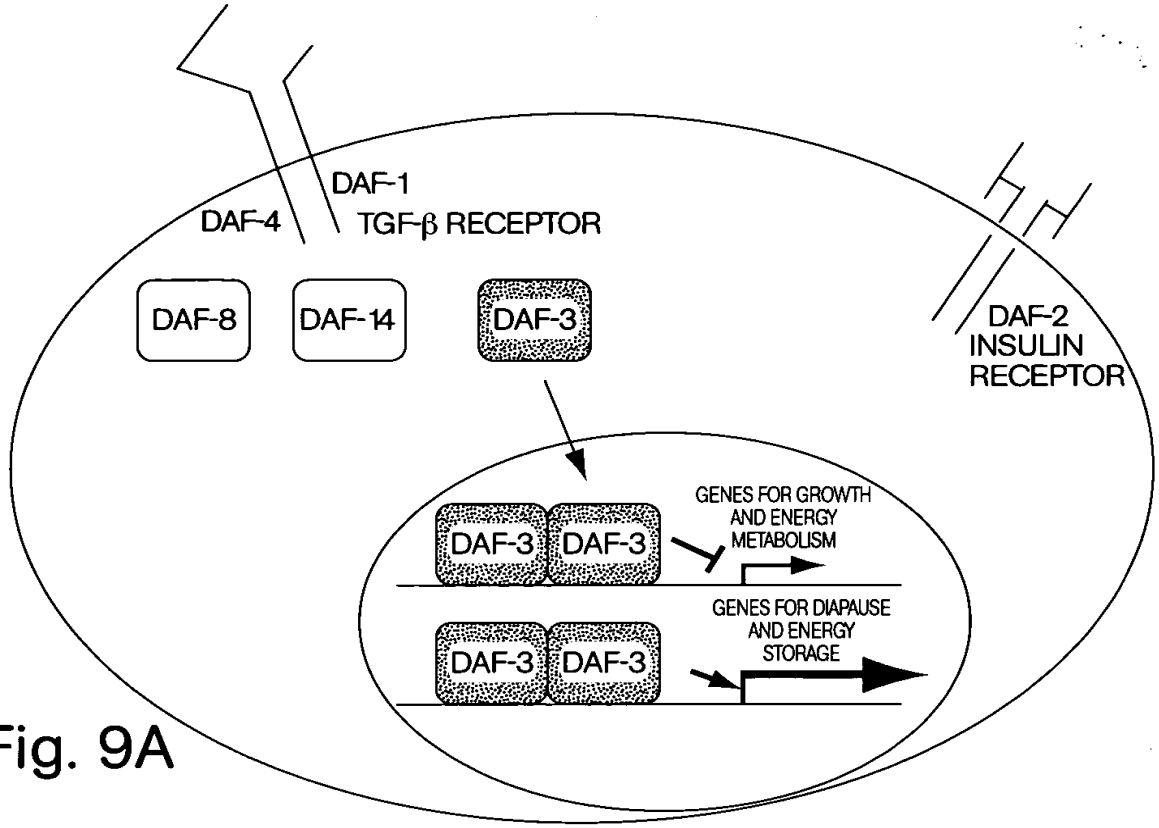
GFP
nerve cord
nuclei
DAPI

Fig. 8B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DAF-4
TGF-β RECEPTOR
DAF-8
DAF-14
DAF-3
DAF-2
INSULIN
RECEPTOR
DAF-3
DAF-3
GENES FOR GROWTH
AND ENERGY
METABOLISM
DAF-3
DAF-3
GENES FOR DIAPAUSE
AND ENERGY
STORAGE

Fig. 9A

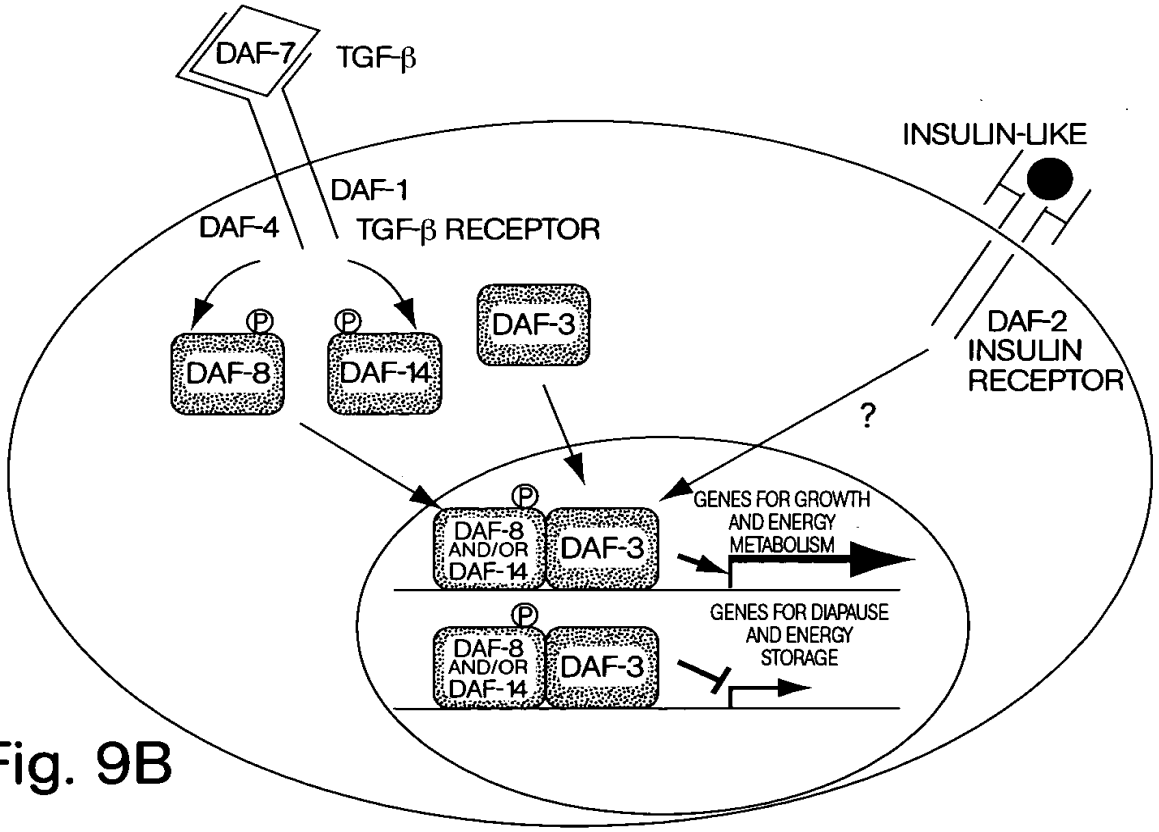
DAF-7
TGF-β
INSULIN-LIKE
DAF-1
DAF-4
TGF-β RECEPTOR
P
DAF-8
P
DAF-14
DAF-3
DAF-2
INSULIN
RECEPTOR
?
P
DAF-8
AND/OR
DAF-14
DAF-3
GENES FOR GROWTH
AND ENERGY
METABOLISM
P
DAF-8
AND/OR
DAF-14
DAF-3
GENES FOR DIAPAUSE
AND ENERGY
STORAGE

Fig. 9B

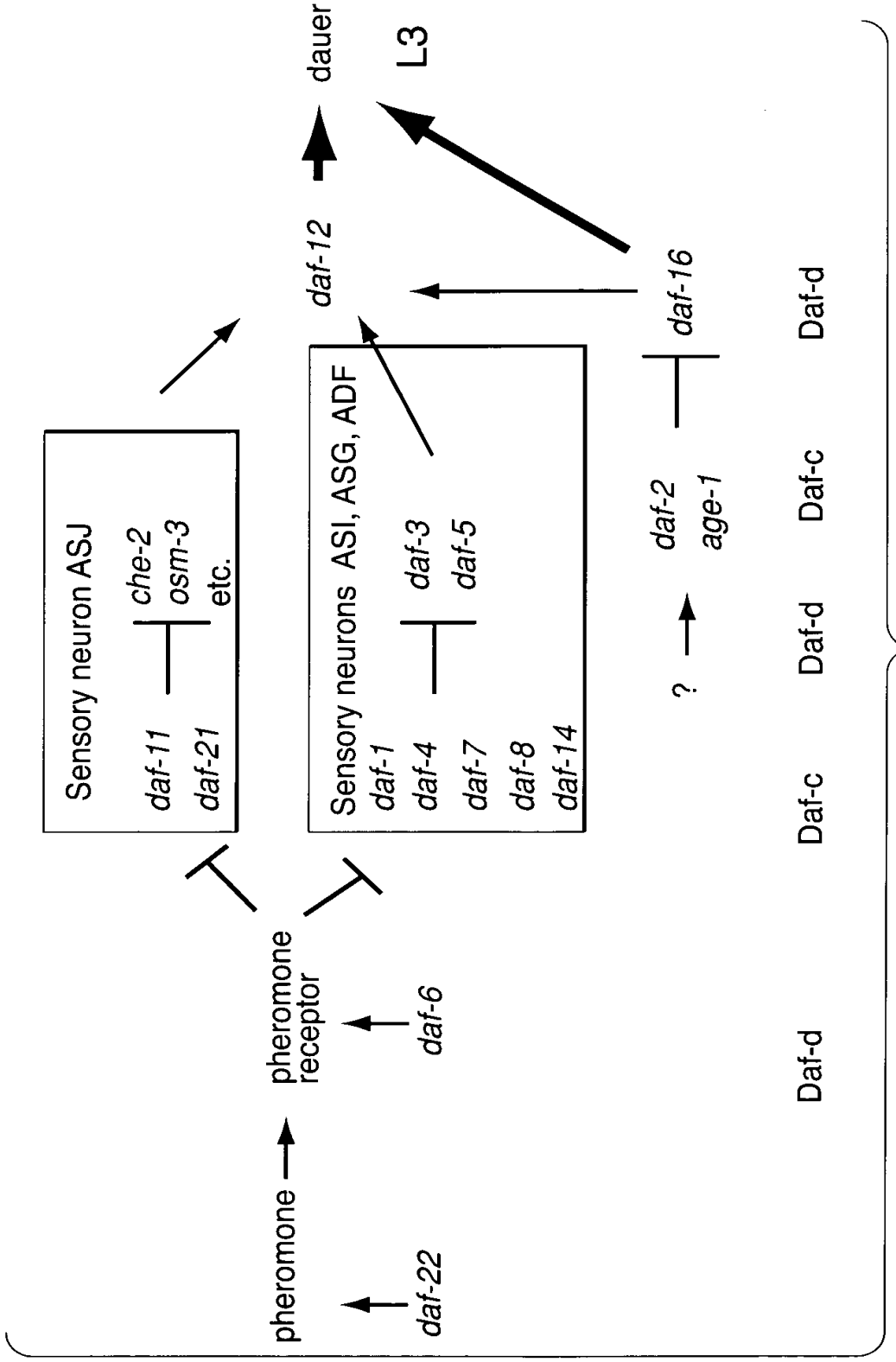
pheromone
daf-22
pheromone receptor
daf-6
Sensory neuron ASJ
daf-11
daf-21
che-2
osm-3
etc.
Sensory neurons ASI, ASG, ADF
daf-1
daf-4
daf-7
daf-8
daf-14
daf-3
daf-5
daf-12
?
daf-2
age-1
daf-16
dauer
L3
Daf-d
Daf-c
Daf-d
Daf-c
Daf-d

Fig. 10

```
   1  atgaagctaa tagcaacttc tcttctagtt cccgacgagc acacaccgat
  51  gatgtcacca gtgaatacaa ctacaaagat tctacaacgg agtggtatta
 101  aaatggaaat cccgccatat ttggatccag acagtcagga tgatgacccg
 151  gaagatggtg tcaactaccc ggatccagat ttatttgaca caaaaaacac
 201  aaatatgacc gagtacgatt tggatgtgtt gaagcttgga aaaccagcag
 251  tagatgaagc acggaaaaag atcgaagttc ccgacgctag tgcgccgcca
 301  aacaaaattg tagaatattt gatgtattat agaacgttaa aagaaagtga
 351  actcatacaa ctgaatgcgt atcggacaaa acgaaatcga ttatcgttga
 401  acttggtcaa aaacaatatt gatcgagagt tcgaccaaaa agcttgcgag
 451  tccctggtga aaaaattgaa ggataagaag aatgatctcc agaacctgat
 501  tgatgtggtt ctttcaaaag gtacaaaata taccggttgc attacaattc
 551  caaggacact tgatggccgg ttacaggtcc acggaagaaa aggtttccct
 601  cacgtagtct atggcaaact gtggaggttt aatgaaatga caaaaaacga
 651  aacgcgtcat gtggaccact gcaagcacgc atttgaaatg aaaagtgaca
 701  tggtatgcgt gaatccctat cactacgaaa ttgtcattgg aactatgatt
 751  gttgggcaga gggatcatga caatcgagat atgccgccgc cacatcaacg
 801  ctaccacact ccaggtcggc aggatccagt tgacgatatg agtagattta
 851  taccaccagc ttccattcgt ccgcctccga tgaacatgca cacaaggcct
 901  cagcctatgc ctcaacaatt gccttcagtt ggcgcaacgt ttgcccatcc
 951  tctcccacat caggcgccac ataacccagg ggtttcacat ccgtactcca
1001  ttgctccaca gacccattac ccgttgaaca tgaacccaat tccgcaaatg
1051  ccgcaaatgc cacaaatgcc accacctctc catcagggat atggaatgaa
1101  tgggccgagt tgctcttcag aaaacaacaa tccattccac caaaatcacc
1151  attataatga tattagccat ccaaatcact attcctacga ctgtggtccg
1201  aacttgtacg ggtttccaac tccttatccg gattttcacc atcctttcaa
1251  tcagcaacca caccagccgc cacaactatc acaaaaccat acgtcccaac
1301  aaggcagtca tcaaccaggg caccaaggtc aggtaccgaa tgatccacca
1351  atttcaagac cagtgttaca accatcaaca gtcaccttgg acgtgttccg
1401  tcggtactgt agacagacat ttggaaatcg atttttgaa ggagaaagtg
1451  aacaatccgg cgcaataatt cggtctagta acaaattcat tgaagaattt
1501  gattcgccga tttgtggtgt gacagttgtt cgaccgcgga tgacagacgg
1551  tgaggttttg gagaacatca tgccggaaga tgcaccatat catgacattt
1601  gcaagttcat tttgaggctc acatcagaaa gtgtaacttt ctcaggagag
1651  gggccagaag ttagtgattt gaacgaaaaa tggggaacaa ttgtgtacta
1701  tgagaaaaat ttgcaaattg gcgagaaaaa atgttcgaga ggaaatttcc
1751  acgtggatgg cggattcatt tgctctgaga atcgttacag tctcggactt
1801  gagccaaatc caattagaga accagtggcg tttaaagttc gtaaagcaat
1851  agtggatgga attcgctttt cctacaaaaa agacgggagt gtttggcttc
1901  aaaaccgcat gaagtacccg gtatttgtca cttctgggta tctcgacgag
1951  caatcaggag gcctaaagaa ggataaagtg cacaaagttt acggatgtgc
2001  gtctatcaaa acgtttggct tcaacgtttc caaacaaatc atcagagacg
2051  cgcttctttc caagcaaatg gcaacaatgt acttgcaagg aaaattgact
```

Fig. 11A (sheet 1 of 2)

```
2101  ccgatgaatt atatctacga gaagaagact caggaagagc tgcgaaggga
2151  agcaacacgc accactgatt cattggccaa gtactgttgt gtccgtgtct
2201  cgttctgcaa aggatttgga gaagcatacc cagaacgccc gtcaattcat
2251  gattgtccag tttggattga gttgaaaatc aacattgcct acgatttcat
2301  ggattcaatc tgccagtaca taaccaactg cttcgagccg ctaggaatgg
2351  aagattttgc aaaattggga atcaacgtca gtgatgacta aatgataact
2401  tttttcactc accctactag atactgattt agtcttattc caaatcatcc
2451  aacgatatca aacttttcc tttgaacttt gcatactatg ttatcacaag
2501  ttccaagcag tttcaataca aacataggat atgttaacaa cttttgataa
2551  gaatcaagtt accaactgtt cattgtgagc tttgagctgt atagaaggac
2601  aatgtatccc atacctcaat ctttaatagt catcagtcac tggtcccgca
2651  ccaatttttt cgattcgcat atgtcatata ttgcaccgtg gccctttta
2701  ttgtaacttt taatatattt tcttcccaac ttgtgaatat gattgatgaa
2751  ccaccatttt gagtaataaa tgtatttttt gtgg
```

Fig. 11A (sheet 2 of 2)

```
   1  gtaatcaaat tgtaaaggaa aaatattaat agtcagagta cacataaatg
  51  ggtgatcatc ataatttaac gggccttccc ggtacctcca tcccgccaca
 101  gttcaactat tctcagcccg gtaccagcac cggaggcccg ctttatggtg
 151  gaaaaccttc tcatggattg gaagatattc ctgatgtaga ggaatatgag
 201  aggaacctgc tcggggctgg agcaggtttt aatctgctca atgtaggaaa
 251  tatggctaat gttcccgacg agcacacacc gatgatgtca ccagtgaata
 301  caactacaaa gattctacaa cggagtggta ttaaaatgga aatcccgcca
 351  tatttggatc cagacagtca ggatgatgac ccggaagatg gtgtcaacta
 401  cccggatcca gatttatttg acacaaaaaa cacaaatatg accgagtacg
 451  atttggatgt gttgaagctt ggaaaaccag cagtagatga agcacggaaa
 501  aagatcgaag ttcccgacgc tagtgcgccg ccaaacaaaa ttgtagaata
 551  tttgatgtat tatagaacgt taaaagaaag tgaactcata caactgaatg
 601  cgtatcggac aaaacgaaat cgattatcgt tgaacttggt caaaaacaat
 651  attgatcgag agttcgacca aaaagcttgc gagtccctgg tgaaaaaatt
 701  gaaggataag aagaatgatc tccagaacct gattgatgtg gttctttcaa
 751  aaggtacaaa atataccggt tgcattacaa ttccaaggac acttgatggc
 801  cggttacagg tccacggaag aaaaggtttc cctcacgtag tctatggcaa
 851  actgtggagg tttaatgaaa tgacaaaaaa cgaaacgcgt catgtggacc
 901  actgcaagca cgcatttgaa atgaaaagtg acatggtatg cgtgaatccc
 951  tatcactacg aaattgtcat tggaactatg attgttgggc agagggatca
1001  tgacaatcga gatatgccgc cgccacatca acgctaccac actccaggtc
1051  ggcaggatcc agttgacgat atgagtagat ttataccacc agcttccatt
1101  cgtccgcctc cgatgaacat gcacacaagg cctcagccta tgcctcaaca
1151  attgccttca gttggcgcaa cgtttgccca tcctctccca catcaggcgc
1201  cacataaccc aggggtttca catccgtact ccattgctcc acagacccat
1251  tacccgttga acatgaaccc aattccgcaa atgccgcaaa tgccacaaat
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1451  aactccttat ccggattttc accatccttt caatcagcaa ccacaccagc
1501  cgccacaact atcacaaaac catacgtccc aacaaggcag tcatcaacca
1551  gggcaccaag gtcaggtacc gaatgatcca ccaatttcaa gaccagtgtt
1601  acaaccatca acagtcacct tggacgtgtt ccgtcggtac tgtagacaga
1651  catttggaaa tcgatttttt gaaggagaaa gtgaacaatc cggcgcaata
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1751  tgtgacagtt gttcgaccgc ggatgacaga cggtgaggtt ttggagaaca
1801  tcatgccgga agatgcacca tatcatgaca tttgcaagtt catttgagg
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1901  tttgaacgaa aaatggggaa caattgtgta ctatgagaaa aatttgcaaa
1951  ttggcgagaa aaaatgttcg agaggaaatt tccacgtgga tggcggattc
2001  atttgctctg agaatcgtta cagtctcgga cttgagccaa atccaattag
2051  agaaccagtg gcgtttaaag ttcgtaaagc aatagtggat ggaattcgct
```

Fig. 11B (sheet 1 of 2)

```
2101  tttcctacaa aaaagacggg agtgtttggc ttcaaaaccg catgaagtac
2151  ccggtatttg tcacttctgg gtatctcgac gagcaatcag gaggcctaaa
2201  gaaggataaa gtgcacaaag tttacggatg tgcgtctatc aaaacgtttg
2251  gcttcaacgt ttccaaacaa atcatcagag acgcgcttct ttccaagcaa
2301  atggcaacaa tgtacttgca aggaaaattg actccgatga attatatcta
2351  cgagaagaag actcaggaag agctgcgaag ggaagcaaca cgcaccactg
2401  attcattggc caagtactgt tgtgtccgtg tctcgttctg caaaggattt
2451  ggagaagcat acccagaacg cccgtcaatt catgattgtc cagtttggat
2501  tgagttgaaa atcaacattg cctacgattt catggattca atctgccagt
2551  acataaccaa ctgcttcgag ccgctaggaa tggaagattt tgcaaaattg
2601  ggaatcaacg tcagtgatga ctaaatgata actttttca ctcaccctac
2651  tagatactga tttagtctta ttccaaatca tccaacgata tcaaactttt
2701  tcctttgaac tttgcatact atgttatcac aagttccaag cagtttcaat
2751  acaaacatag gatatgttaa caacttttga taagaatcaa gttaccaact
2801  gttcattgtg agctttgagc tgtatagaag gacaatgtat cccatacctc
2851  aatctttaat agtcatcagt cactggtccc gcaccaattt tttcgattcg
2901  catatgtcat atattgcacc gtggcccttt ttattgtaac ttttaatata
2951  ttttcttccc aacttgtgaa tatgattgat gaaccaccat tttgagtaat
3001  aaatgtattt tttgtgg
```

Fig. 11B (sheet 2 of 2)

```
   1  gtaatcaaat tgtaaaggaa aaatattaat agtcagagta cacataaatg
  51  ggtgatcatc ataatttaac gggccttccc ggtacctcca tcccgccaca
 101  gttcaactat tctcagcccg gtaccagcac cggaggcccg ctttatggtg
 151  gaaaaccttc tcatggattg gaagatattc ctgatgtaga ggaatatgag
 201  aggaacctgc tcggggctgg agcaggtttt aatctgctca atgtaggaaa
 251  tatggctaat gaatttaaac caataatcac attggacacg aaaccacctc
 301  gtgatgccaa caagtcattg gcattcaatg gcgggttgaa gctaatcact
 351  ccgaaaactg aagttcccga cgagcacaca ccgatgatgt caccagtgaa
 401  tacaactaca aagattctac aacggagtgg tattaaaatg gaaatcccgc
 451  catatttgga tccagacagt caggatgatg acccggaaga tggtgtcaac
 501  tacccggatc cagatttatt tgacacaaaa aacacaaata tgaccgagta
 551  cgatttggat gtgttgaagc ttggaaaacc agcagtagat gaagcacgga
 601  aaaagatcga agttcccgac gctagtgcgc cgccaaacaa aattgtagaa
 651  tatttgatgt attatagaac gttaaaagaa agtgaactca tacaactgaa
 701  tgcgtatcgg acaaaacgaa atcgattatc gttgaacttg gtcaaaaaca
 751  atattgatcg agagttcgac caaaaagctt gcgagtccct ggtgaaaaaa
 801  ttgaaggata agaagaatga tctccagaac ctgattgatg tggttctttc
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 901  gccggttaca ggtccacgga agaaaaggtt tccctcacgt agtctatggc
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1151  tcggcaggat ccagttgacg atatgagtag atttatacca ccagcttcca
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1551  ccaactcctt atccggattt tcaccatcct ttcaatcagc aaccacacca
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1651  cagggcacca aggtcaggta ccgaatgatc caccaatttc aagaccagtg
1701  ttacaaccat caacagtcac cttggacgtg ttccgtcggt actgtagaca
1751  gacatttgga aatcgatttt ttgaaggaga aagtgaacaa tccggcgcaa
1801  taattcggtc tagtaacaaa ttcattgaag aatttgattc gccgatttgt
1851  ggtgtgacag ttgttcgacc gcggatgaca gacggtgagg ttttggagaa
1901  catcatgccg gaagatgcac catatcatga catttgcaag ttcattttga
1951  ggctcacatc agaaagtgta actttctcag gagaggggcc agaagttagt
2001  gatttgaacg aaaaatgggg aacaattgtg tactatgaga aaaatttgca
2051  aattggcgag aaaaaatgtt cgagaggaaa tttccacgtg gatggcggat
```

Fig. 11C (sheet 1 of 2)

```
2101  tcatttgctc tgagaatcgt tacagtctcg gacttgagcc aaatccaatt
2151  agagaaccag tggcgtttaa agttcgtaaa gcaatagtgg atggaattcg
2201  cttttcctac aaaaaagacg ggagtgtttg gcttcaaaac cgcatgaagt
2251  acccggtatt tgtcacttct gggtatctcg acgagcaatc aggaggccta
2301  aagaaggata aagtgcacaa agtttacgga tgtgcgtcta tcaaaacgtt
2351  tggcttcaac gtttccaaac aaatcatcag agacgcgctt ctttccaagc
2401  aaatggcaac aatgtacttg caaggaaaat tgactccgat gaattatatc
2451  tacgagaaga agactcagga agagctgcga agggaagcaa cacgcaccac
2501  tgattcattg gccaagtact gttgtgtccg tgtctcgttc tgcaaaggat
2551  ttggagaagc atacccagaa cgcccgtcaa ttcatgattg tccagtttgg
2601  attgagttga aaatcaacat tgcctacgat ttcatggatt caatctgcca
2651  gtacataacc aactgcttcg agccgctagg aatggaagat tttgcaaaat
2701  tgggaatcaa cgtcagtgat gactaaatga taacttttt cactcaccct
2751  actagatact gatttagtct tattccaaat catccaacga tatcaaactt
2801  tttcctttga actttgcata ctatgttatc acaagttcca agcagtttca
2851  atacaaacat aggatatgtt aacaactttt gataagaatc aagttaccaa
2901  ctgttcattg tgagctttga gctgtataga aggacaatgt atcccatacc
2951  tcaatcttta atagtcatca gtcactggtc ccgcaccaat tttttcgatt
3001  cgcatatgtc atatattgca ccgtggccct ttttattgta acttttaata
3051  tattttcttc ccaacttgtg aatatgattg atgaaccacc attttgagta
3101  ataaatgtat tttttgtgg
```

Fig. 11C (sheet 2 of 2)

```
  1  MKLIATSLLV PDEHTPMMSP VNTTTKILQR SGIKMEIPPY LDPDSQDDDP
 51  EDGVNYPDPD LFDTKNTNMT EYDLDVLKLG KPAVDEARKK IEVPDASAPP
101  NKIVEYLMYY RTLKESELIQ LNAYRTKRNR LSLNLVKNNI DREFDQKACE
151  SLVKKLKDKK NDLQNLIDVV LSKGTKYTGC ITIPRTLDGR LQVHGRKGFP
201  HVVYGKLWRF NEMTKNETRH VDHCKHAFEM KSDMVCVNPY HYEIVIGTMI
251  VGQRDHDNRD MPPPHQRYHT PGRQDPVDDM SRFIPPASIR PPPMNMHTRP
301  QPMPQQLPSV GATFAHPLPH QAPHNPGVSH PYSIAPQTHY PLNMNPIPQM
351  PQMPQMPPPL HQGYGMNGPS CSSENNNPFH QNHHYNDISH PNHYSYDCGP
401  NLYGFPTPYP DFHHPFNQQP HQPPQLSQNH TSQQGSHQPG HQGQVPNDPP
451  ISRPVLQPST VTLDVFRRYC RQTFGNRFFE GESEQSGAII RSSNKFIEEF
501  DSPICGVTVV RPRMTDGEVL ENIMPEDAPY HDICKFILRL TSESVTFSGE
551  GPEVSDLNEK WGTIVYYEKN LQIGEKKCSR GNFHVDGGFI CSENRYSLGL
601  EPNPIREPVA FKVRKAIVDG IRFSYKKDGS VWLQNRMKYP VFVTSGYLDE
651  QSGGLKKDKV HKVYGCASIK TFGFNVSKQI IRDALLSKQM ATMYLQGKLT
701  PMNYIYEKKT QEELRREATR TTDSLAKYCC VRVSFCKGFG EAYPERPSIH
751  DCPVWIELKI NIAYDFMDSI CQYITNCFEP LGMEDFAKLG INVSDD
```

Fig. 12A

```
  1 MGDHHNLTGL PGTSIPPQFN YSQPGTSTGG PLYGGKPSHG LEDIPDVEEY
 51 ERNLLGAGAG FNLLNVGNMA NVPDEHTPMM SPVNTTTKIL QRSGIKMEIP
101 PYLDPDSQDD DPEDGVNYPD PDLFDTKNTN MTEYDLDVLK LGKPAVDEAR
151 KKIEVPDASA PPNKIVEYLM YYRTLKESEL IQLNAYRTKR NRLSLNLVKN
201 NIDREFDQKA CESLVKKLKD KKNDLQNLID VVLSKGTKYT GCITIPRTLD
251 GRLQVHGRKG FPHVVYGKLW RFNEMTKNET RHVDHCKHAF EMKSDMVCVN
301 PYHYEIVIGT MIVGQRDHDN RDMPPPHQRY HTPGRQDPVD DMSRFIPPAS
351 IRPPPMNMHT RPQPMPQQLP SVGATFAHPL PHQAPHNPGV SHPYSIAPQT
401 HYPLNMNPIP QMPQMPQMPP PLHQGYGMNG PSCSSENNNP FHQNHHYNDI
451 SHPNHYSYDC GPNLYGFPTP YPDFHHPFNQ QPHQPPQLSQ NHTSQQGSHQ
501 PGHQGQVPND PPISRPVLQP STVTLDVFRR YCRQTFGNRF FEGESEQSGA
551 IIRSSNKFIE EFDSPICGVT VVRPRMTDGE VLENIMPEDA PYHDICKFIL
601 RLTSESVTFS GEGPEVSDLN EKWGTIVYYE KNLQIGEKKC SRGNFHVDGG
651 FICSENRYSL GLEPNPIREP VAFKVRKAIV DGIRFSYKKD GSVWLQNRMK
701 YPVFVTSGYL DEQSGGLKKD KVHKVYGCAS IKTFGFNVSK QIIRDALLSK
751 QMATMYLQGK LTPMNYIYEK KTQEELRREA TRTTDSLAKY CCVRVSFCKG
801 FGEAYPERPS IHDCPVWIEL KINIAYDFMD SICQYITNCF EPLGMEDFAK
851 LGINVSDD
```

Fig. 12B

```
  1 MGDHHNLTGL PGTSIPPQFN YSQPGTSTGG PLYGGKPSHG LEDIPDVEEY
 51 ERNLLGAGAG FNLLNVGNMA NEFKPIITLD TKPPRDANKS LAFNGGLKLI
101 TPKTEVPDEH TPMMSPVNTT TKILQRSGIK MEIPPYLDPD SQDDDPEDGV
151 NYPDPDLFDT KNTNMTEYDL DVLKLGKPAV DEARKKIEVP DASAPPNKIV
201 EYLMYYRTLK ESELIQLNAY RTKRNRLSLN LVKNNIDREF DQKACESLVK
251 KLKDKKNDLQ NLIDVVLSKG TKYTGCITIP RTLDGRLQVH GRKGFPHVVY
301 GKLWRFNEMT KNETRHVDHC KHAFEMKSDM VCVNPYHYEI VIGTMIVGQR
351 DHDNRDMPPP HQRYHTPGRQ DPVDDMSRFI PPASIRPPPM NMHTRPQPMP
401 QQLPSVGATF AHPLPHQAPH NPGVSHPYSI APQTHYPLNM NPIPQMPQMP
451 QMPPPLHQGY GMNGPSCSSE NNNPFHQNHH YNDISHPNHY SYDCGPNLYG
501 FPTPYPDFHH PFNQQPHQPP QLSQNHTSQQ GSHQPGHQGQ VPNDPPISRP
551 VLQPSTVTLD VFRRYCRQTF GNRFFEGESE QSGAIIRSSN KFIEEFDSPI
601 CGVTVVRPRM TDGEVLENIM PEDAPYHDIC KFILRLTSES VTFSGEGPEV
651 SDLNEKWGTI VYYEKNLQIG EKKCSRGNFH VDGGFICSEN RYSLGLEPNP
701 IREPVAFKVR KAIVDGIRFS YKKDGSVWLQ NRMKYPVFVT SGYLDEQSGG
751 LKKDKVHKVY GCASIKTFGF NVSKQIIRDA LLSKQMATMY LQGKLTPMNY
801 IYEKKTQEEL RREATRTTDS LAKYCCVRVS FCKGFGEAYP ERPSIHDCPV
851 WIELKINIAY DFMDSICQYI TNCFEPLGME DFAKLGINVS DD
```

Fig. 12C

tgatctttcaagccgaagcaatcaagacctcaaagccaatcaactctactcacttttcttcagaaccttaacttttttgtg
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Fig. 13A

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Fig. 13B

MMEMLVDQGTDASSSASTSTSSVSRFGADTFMNTPDDVMMNDDMEPIPRDR
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TTAIMASPEKRLTLAQVYEWMVQNVPYFRDKGDSNSSAGWKNSIRHNLSLH
SRFMRIQNEGAGKSSWWVINPDAKPGMNPRRTRERSNTIETTTKAQLEKSR
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Fig. 14A

MQQYIYQESSATIPHHHLNQHNNPYHPMHPHHQLPHMQQLPQPLLNLNMTT
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FRPRTQSNLSIPGSSSRVSPAIGSDIYDDLEFPSWVGESVPAIPSDIVDRT
DQMRIDATTHIGGVQIKQESKPIKTEPIAPPPSYHELNSVRGSCAQNPLLR
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Fig. 14B

```
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  61 cagatgcatg ttaacatttt acatccacaa ctgcaaacga tggtcgagca gtggcaaatg
 121 cgagaacgcc catcgctgga gaccgagaat ggcaaaggat cgctgctcct ggaaaatgaa
 181 ggtgtcgcag atatcatcac tatgtgtcca ttcggagaag ttattagtgt agtatttccg
 241 tggtttcttg caaatgtgcg aacatcgcta gaaatcaagc tatcagattt caaacatcaa
 301 cttttcgaat tgattgctcc gatgaagtgg ggaacatatt ccgtaaagcc acaggattat
 361 gtgttcagac agttgaataa tttcggcgaa attgaagtta tatttaacga cgatcaaccc
 421 ctgtcgaaat tagagctcca cggcactttc ccaatgcttt ttctctacca acctgatgga
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 541 aaactggaag agagcctcga tgaggaactc cgtcaatttc gtgcttctct ctgggctcgt
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 781 gagaaaatga tgaagattca aattgaattc aatccgaacg aaactccgaa atctctgctt
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2521 aaagccatcg tcctaggaag tgcaaaacgt ccgttaatgc ttcactggaa gaacaaaaat
2581 ccaaagagtg acctgcacct tccgttctgt gcaatgatct tcaagaatgg agacgatctt
2641 cgccaggaca tgcttgttct tcaagttctc gaagttatgg ataacatctg gaaggctgca
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Fig. 15 (sheet 1 of 2)

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2701 aacattgatt gctgtttgaa cccgtacgca gttcttccaa tgggagaaat gattggaatt
2761 attgaagttg tgcctaattg taaaacaata ttcgagattc aagttggaac aggattcatg
2821 aatacagcag ttcggagtat tgatccttcg tttatgaata agtggattcg gaaacaatgc
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3481 ttccacgcag tcaaacacta ctga
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Fig. 15 (sheet 2 of 2)

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   1 RKPWSSRSDC WTRTELRRIS QMHVNILHPQ LQTMVEQWQM RERPSLETEN GKGSLLLENE
  61 GVADIITMCP FGEVISVVFP WFLANVRTSL EIKLSDFKHQ LFELIAPMKW GTYSVKPQDY
 121 VFRQLNNFGE IEVIFNDDQP LSKLELHGTF PMLFLYQPDG INRDKELMSD ISHCLGYSLD
 181 KLEESLDEEL RQFRASLWAR TKKTCLTRGL EGTSHYAFPE EQYLCVGESC PKDLESKVKA
 241 AKLSYQMFWR KRKAEINGVC EKMMKIQIEF NPNETPKSLL HTFLYEMRKL DVYDTDDPAD
 301 EGWFLQLAGR TTFVTNPDVK LTSYDGVRSE LESYRCPGFV VRRQSLVLKD YCRPKPLYEP
 361 HYVRAHERKL ALDVLSVSID STPKQSKNSD MVMTDFRPTA SLKQVSLWDL DANLMIRPVN
 421 ISGFDFPADV DMYVRIEFSV YVGTLTLASK STTKVNAQFA KWNKEMYTFD LYMKDMPPSA
 481 VLSIRVLYGK VKLKSEEFEV GWVNMSLTDW RDELRQGQFL FHLWAPEPTA NRSRIGENGA
 541 RIGTNAAVTI EISSYGGRVR MPSQGQYTYL VKHRSTWTET LNIMGDDYES CIRDPGYKKL
 601 QMLVKKHESG IVLEEDEQRH VWMWRRYIQK QEPDLLIVLS ELAFVWTDRE NFSELYVMLE
 661 KWKPPSVAAA LTLLGKRCTD RVIRKFAVEK LNEQLSPVTF HLFILPLIQA LKYEPRAQSE
 721 VGMMLLTRAL CDYRIGHRLF WLLRAEIARL RDCDLKSEEY RRISLLMEAY LRGNEEHIKI
 781 ITRQVDMVDE LTRISTLVKG MPKDVATMKL RDELRSISHK MENMDSPLDP VYKLGEMIID
 841 KAIVLGSAKR PLMLHWKNKN PKSDLHLPFC AMIFKNGDDL RQDMLVLQVL EVMDNIWKAA
 901 NIDCCLNPYA VLPMGEMIGI IEVVPNCKTI FEIQVGTGFM NTAVRSIDPS FMNKWIRKQC
 961 GIEDEKKKSK KDSTKNPIEK KIDNTQAMKK YFESVDRFLY SCVGYSVATY IMGIKDRHSD
1021 NLMLTEDGKY VHIDFGHILG HGKTKLGIQR DRQPFILTEH FMTVIRSGKS VDGNSHELQK
1081 FKTLCVEAYE VMWNNRDLFV SLFTLMLGME LPELSTKADL DHLKKTLFCN GESKEEARKF
1141 FAGIYEEAFN GSWSTKTNWL FHAVKHY
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Fig. 16

CONVERGENT TGF-β AND INSULIN SIGNALING ACTIVATE GLUCOSE-BASED METABOLISM GENES

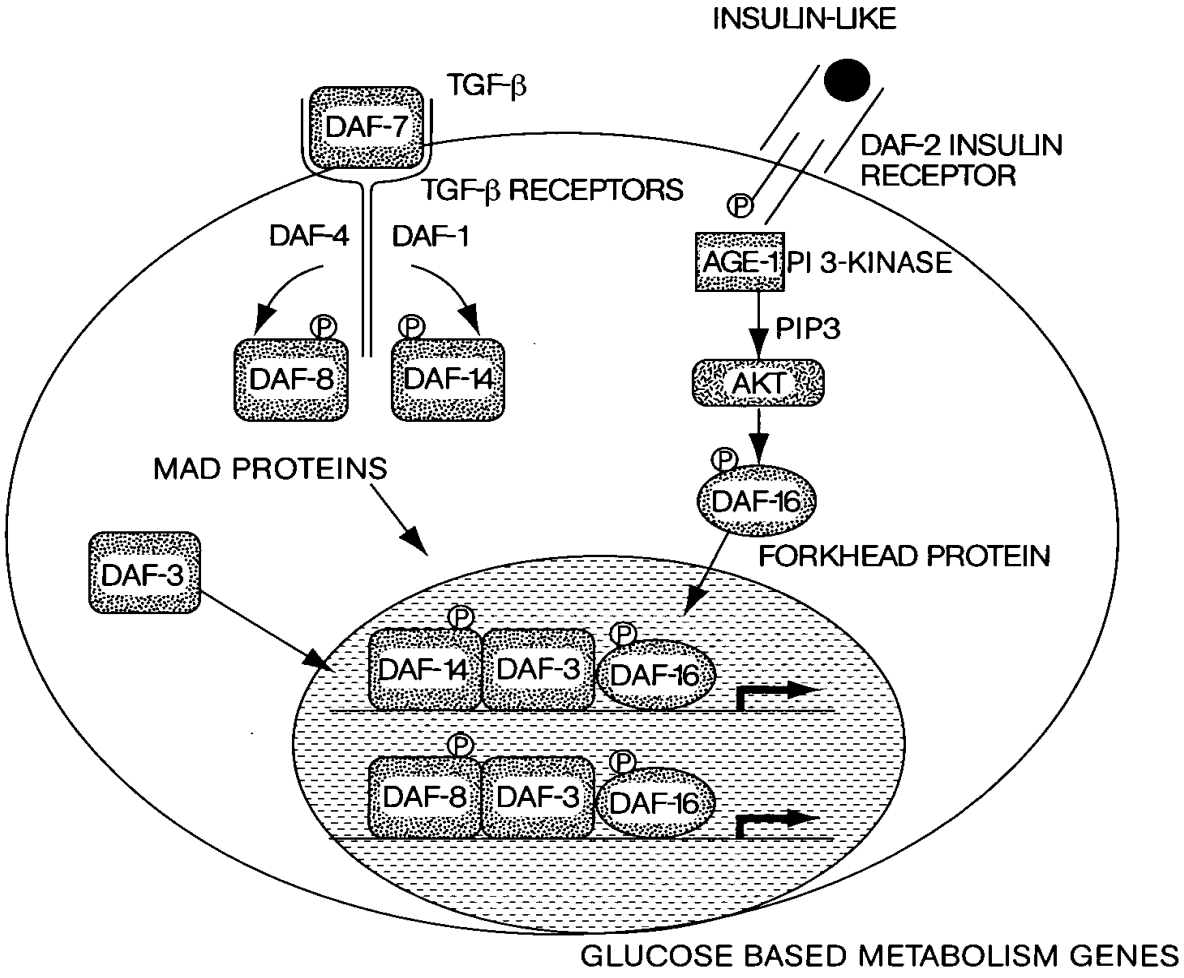


Fig. 17

IN PHEROMONE, NO TGFβ OR INSULIN-LIKE SIGNALS CAUSES REPRESSION OF ANABOLIC GENES

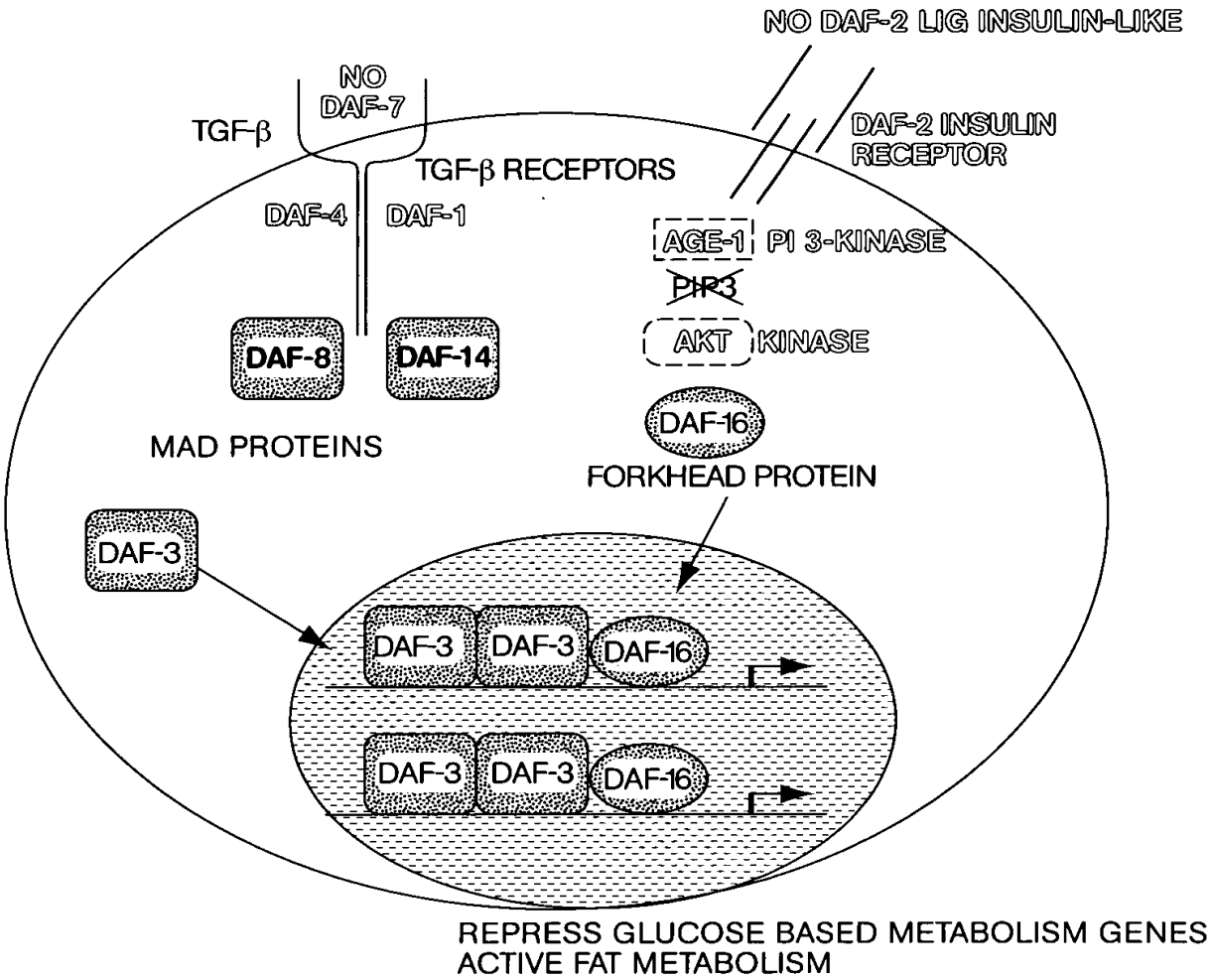
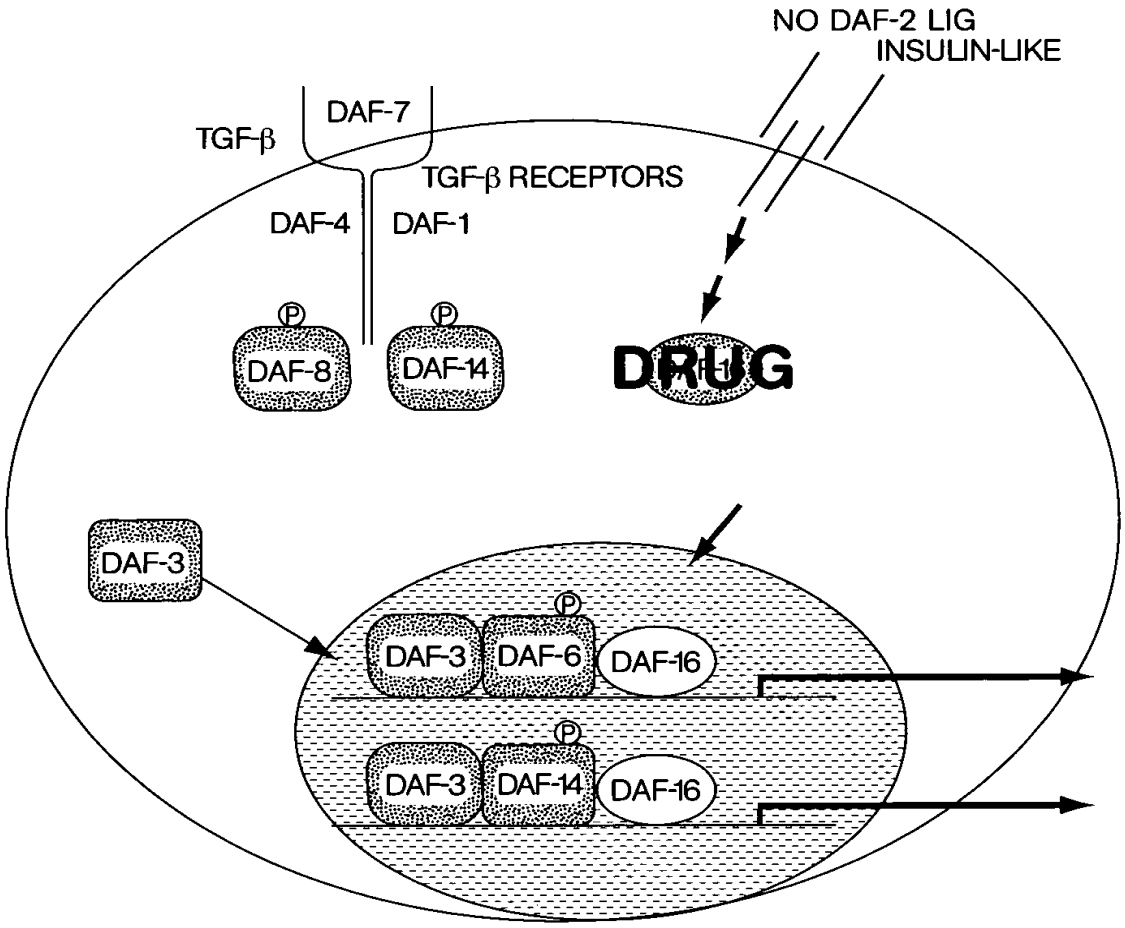


Fig. 18

**DRUGS THAT INHIBIT DAF-16 OR DAF-3
(OR PROTEINS IN THE PATHWAY)
CAN BE DISCOVERED USING REPORTER GENES
BEARING THEIR COGNATE BINDING SITES**



DRUG CAUSES A DECREASE IN DAF-16 ACTIVITY, ACTIVATING
THE REPORTER GENE LIKE A DAF-16 MUTANT.
THIS BYPASSES THE NEED FOR INSULIN

Fig. 19

DRUGS THAT INHIBIT DAF-3 WILL CURE THE DIABETES CAUSED BY A LACK OF DAF-7

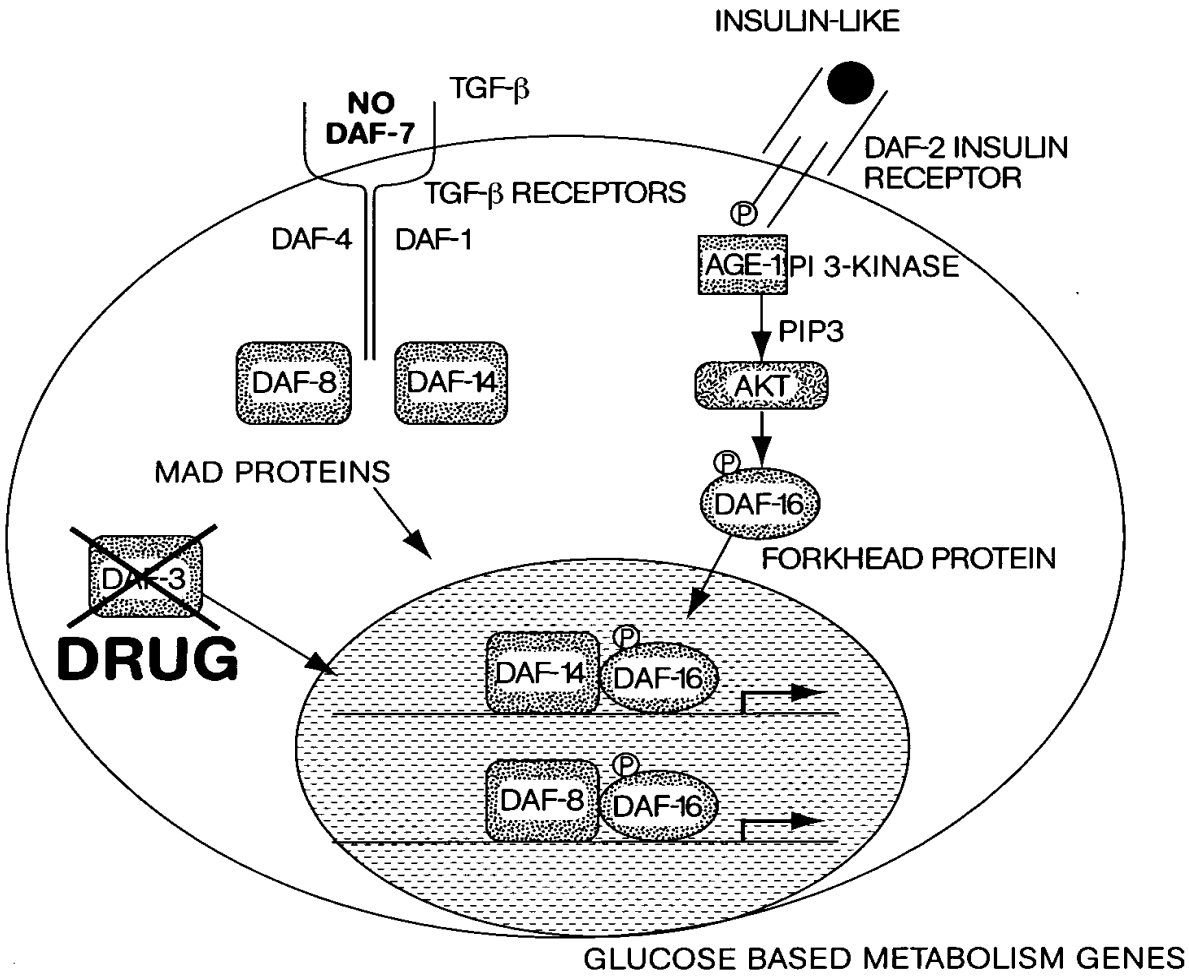


Fig. 20

```
DAF-16a1    1 ------------------------------MMEMLVDQGTDASSSASTSTSSVSRFGADTFMNTPDDVMMNDDMEPIPRDR
DAF-16b     1 -------------MNDSIDDDFPPEPRGRCYTWPMQQYIYQESSATIPHHHLNQHNNPYHPMHPHHQLPHMQQLPQPLLN
FKHR        1 --------MAEAPQVVEIDPDFEPLPRPRSCTWPLPRPEFSQSNSATSSPAPSGSAAAN.........PDAAAGLPSASA
FKHRL1      1 MAEAPASPAPLSPLEVELDPEFEPQSRPRSCTWPLQRPELQASPAKPSGETAADSMIPE.........EEDDEDDEDGGG
AFX         1-----------------------------------------------------------------------MRIQPQKAA

DAF-16a1   52 CN..TWPMRRPQLEPPLNSSPIIHEQIPEEDADLYGSNEQ...CGQLGGASSNGSTAMLHTPDGSNSHQTSFPSDFRMSE
DAF-16b    68 LNMTTLTSSGSSVASSIGGGAQCSPCASGSSTAATNSSQQQQTVGQMLAASVPCSSSGMTLGMSLNLSQGGGPMPAKKKR
FKHR       64 AAVSADFMSNLSLLEESEDFPQAPGSVAAAVAAAAAAAATGGLCGDFQGPEAGC.LHPAPPQPPPPGPLSQHPPVPPAAA
FKHRL1     72 RAGSAMAIGGGGGSGTLGSGLLLEDS..ARVLAPGGQDPGSGPATAAGGLSGGT.QALLQPQQPLP......PPQPGAAG
AFX        10 AIIDLDPDFEPQSRPRSCTWPLPRPEIANQPSEPPEVEPDLGEKVHTEGRSEPI.LLPSRLSEPAGGP...QPGILGAVT

DAF-16a1  127 SPDDTVSGKKTTTRRNAWGNMSYAELITTAIMASPEKRLTLAQVYEWMVQNVPYFRDKGDSNSSAGWKNSIRHNLSLHSR
DAF-16b   148 CRKKP.TDQLAQKKPNPWGEESYSDIIAKALESAPDGRLKLNEIYQWFSDNIPYFGERSSPEEAAGWKNSIRHNLSLHSR
FKHR      143 GPLAGQPRKSSSSRRNAWGNLSYADLITKAIESSAEKRLTLSQIYEWMVKSVPYFKDKGDSNSSAGWKNSIRHNLSLHSK
FKHRL1    143 G..SGQPRK.CSSRRNAWGNLSYADLITRAIESSPDKRLTLSQIYEWMVRCVPYFKDKGDSNSSAGWKNSIRHNLSLHSR
AFX        86 GPRKG......GSRRNAWGNQSYAEFISQAIESAPEKRLTLAQIYEWMVRTVPYFKDKGDSNSSAGWKNSIRHNLSLHSK

DAF-16a1  207 FMRIQNEGAGKSSWWVINPDAKPGRNPRRTRERSNTIETTTKAQLEKSRRGAKKRIKERALMGSLHSTLNGNSIAGSIQT
DAF-16b   227 FMRIQNEGAGKSSWWVINPDAKPGRNPRRTRERSNTIETTTKAQLEKSRRGAKKRIKERALMGSLHSTLNGNSIAGSIQT
FKHR      223 FIRVQNEGTGKSSWWMLNPEG..GKSGKSPRRRAASMDNNSKFAKSRSRAAKKK.......AS.LQSGQEGA.GDSPGSQ
FKHRL1    220 FMRVQNEGTGKSSWWIINPDG..GKSGKAPRRRAVSMDNSNKYTKSRGRAAKKK.......AA.LQTAPESA.DDSP.SQ
AFX       160 FIKVHNEATGKSSWWMLNPEG..GKSGKAPRRRAASMDSSSKLLRGRSKAPKKK.......PSVLPAPPEGATPTSPVGH

DAF-16a1  287 ISHDLYDDDSMQGAFDNVPSSFRPRTQSNLSIPGSSSRVSPAIGSDIYDDL.EFPSWVGESVPAIPSDIVDRTDQMRIDA
DAF-16b   307 ISHDLYDDDSMQGAFDNVPSSFRPRTQSNLSIPGSSSRVSPAIGSDIYDDL.EFPSWVGESVPAIPSDIVDRTDQMRIDA
FKHR      292 FSKWPASPGSHSNDDFDNWSTFRPRTSSNAS..TISGRLSPIM..TEQDDLGEGD..VHSMVYPPSAAKMAST.......
FKHRL1    288 LSKWPGSPTSRSSDELDAWTDFRSRTNSNAS..TVSGRLSPIMASTELDEVQDDDAPLSPMLYSSSASLSPSVSKPCTVE
AFX       231 FAKWSGSPCSRNREEADMWTTFRPRSSSNAS..SVSTRLSPLRPESEV.LAEEIPASVSSYAGGVPPTLNEGLELLDGLN

DAF-16a1  366 TTHIGGVQIKQESKPIKTEPIAPPPSYHELNSVRGSCAQNPLLRNPIVPSTNFKPMPLPGAYGNYQNGGITPINWLSTSN
DAF-16b   386 TTHIGGVQIKQESKPIKTEPIAPPPSYHELNSVRGSCAQNPLLRNPIVPSTNFKPMPLPGAYGNYQNGGITPINWLSTSN
FKHR      359 LPSLSEISNPENM.ENLLDNL.NLLSSPTSLTVSTQSSPGTMMQQTPCYSFAPP.NTSLNSPSPNYQKYTYGQSSMSPLP
FKHRL1    366 LPRLTDMAGTMNLNDGLTENLMDDLLDNITLPPSQPSPTGGLMQRSSSFPYTTK.GSGLGSPTSSFNSTVFGPSSLNSLR
AFX       308 LTSSHSLLSRSGLSGFSLQHPGVTGPLHTYSSSLFSPAEGPLSAGEGCFSSSQALEALLTSDTPPPPADVLMTQVDPILS

DAF-16a1  446 SSPLPGIQS..CGIVAAQHTVASSSALPIDLENLTLPDQPLMDTMDVDALIRHELSQAGGQHIHFDL-------------
DAF-16b   466 SSPLPGIQS..CGIVAAQHTVASSSALPIDLENLTLPDQPLMDTMDVDALIRHELSQAGGQHIHFDL-------------
FKHR      436 QMPIQTLQDNK.SSYGGMSQYNCAPGLLKELLTSDSPPHNDI.MTPVDPGVAQPNSRVLGQNV...MMGPNSVMSTYGSQ
FKHRL1    445 QSPMQTIQENKPATFSSMSHY..GNQTLQDLLTSDSLSHSDVMMTQSDPLMSQASTAVSAQNSRRNVMLRNDPMMSFAAQ
AFX       388 QAPTLLLLGGLPSS....SKLATGVGLCPKPLEARGPSSLVPTLSMIAPPPVMASAPIPKALGTPVLTPPTEAASQDRMP
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Fig. 21A (sheet 1 of 2)

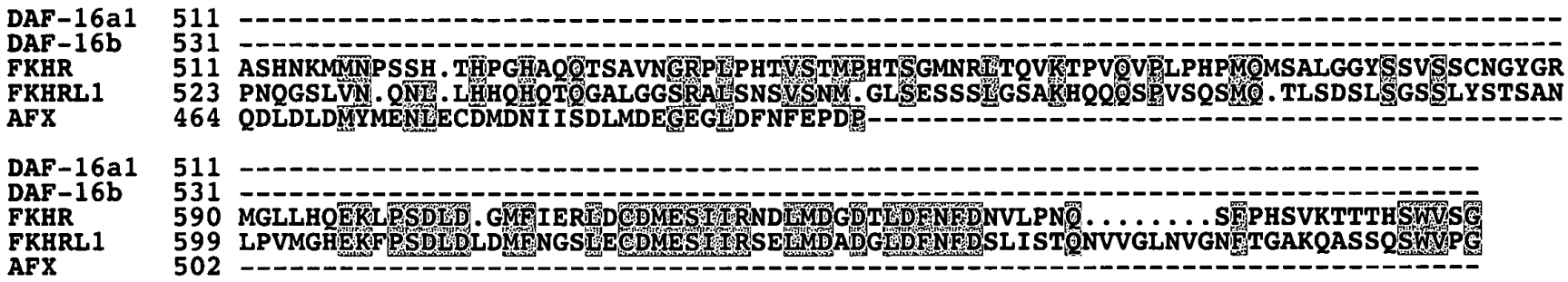
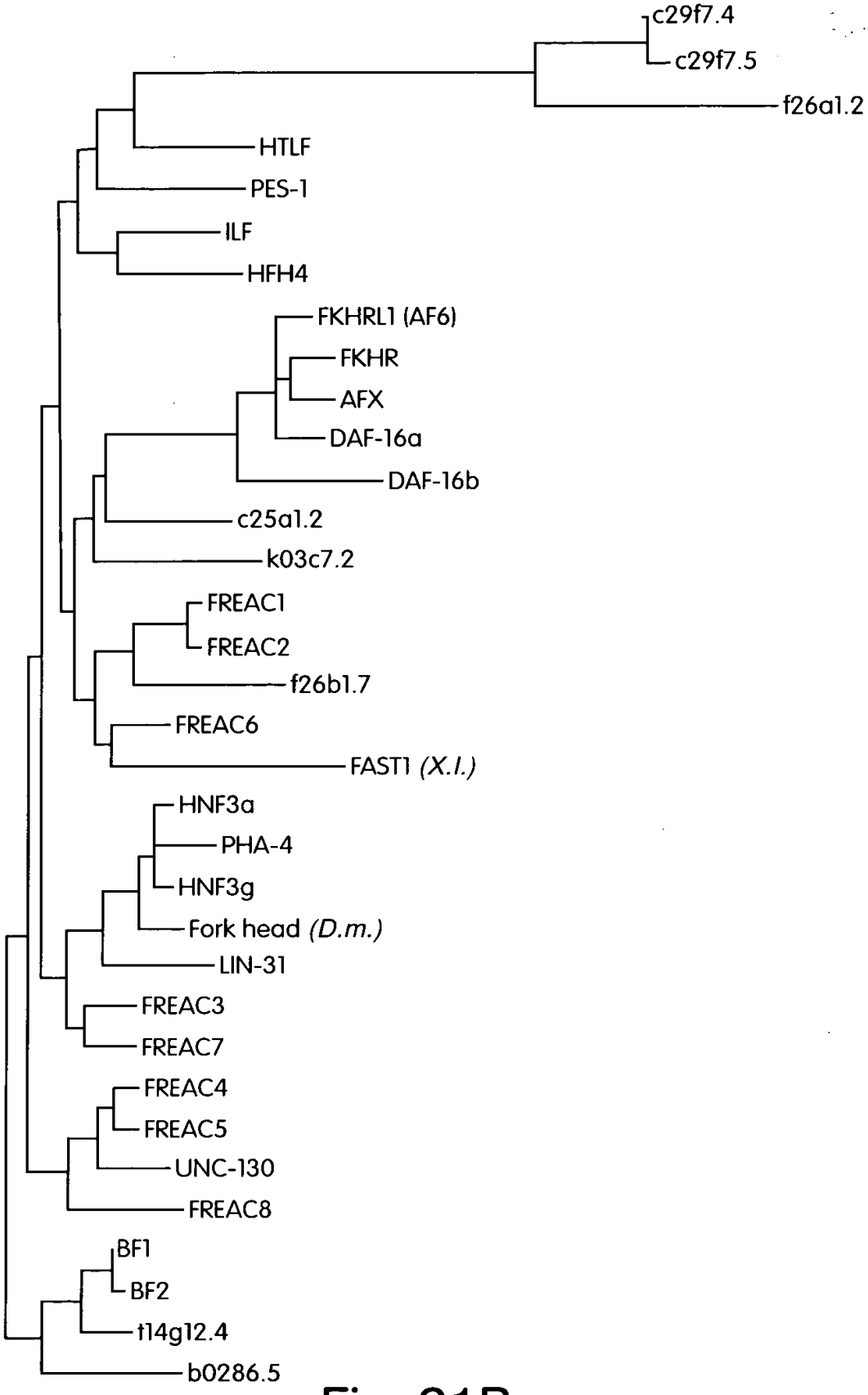


Fig. 21A (sheet 2 of 2)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FKHR
AFX
DAF-16a
DAF-16b
c25a1.2
k03c7.2
FREAC1
FREAC2
f26b1.7
FREAC6
FAST1 (X.l.)
HNF3a
PHA-4
HNF3g
Fork head (D.m.)
LIN-31
FREAC3
FREAC7
FREAC4
FREAC5
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FREAC8
BF1
BF2
t14g12.4
b0286.5

Fig. 21B

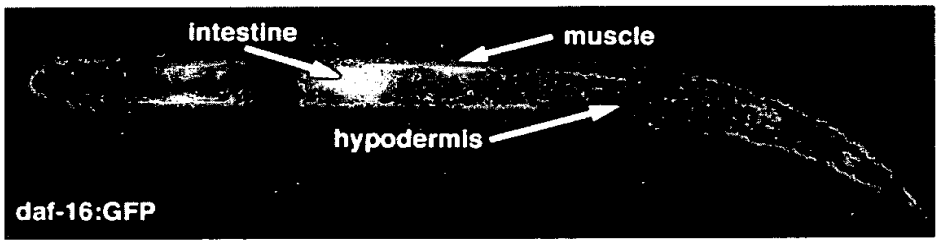
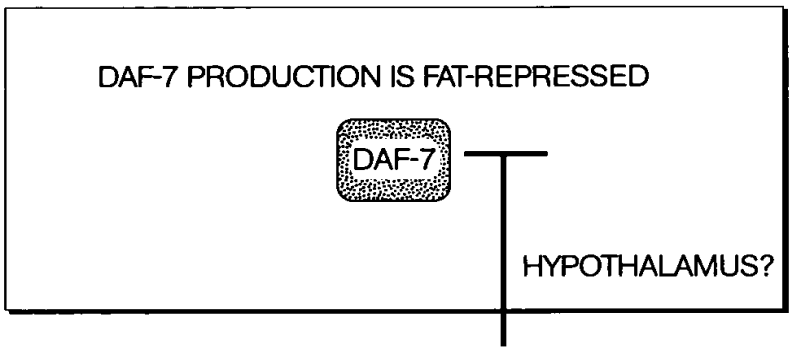


Fig. 22

INJECTION OF OF DAF-7 BYPASSES OBESITY-INDUCED DEFECTS IN INSULIN-REGULATION OF METABOLISM



FATTY ACIDS IN BLOOD REPRESS DAF-7 IN ANALOGY TO PHEROMONE REGULATION OF DAF-7 IN C. ELEGANS

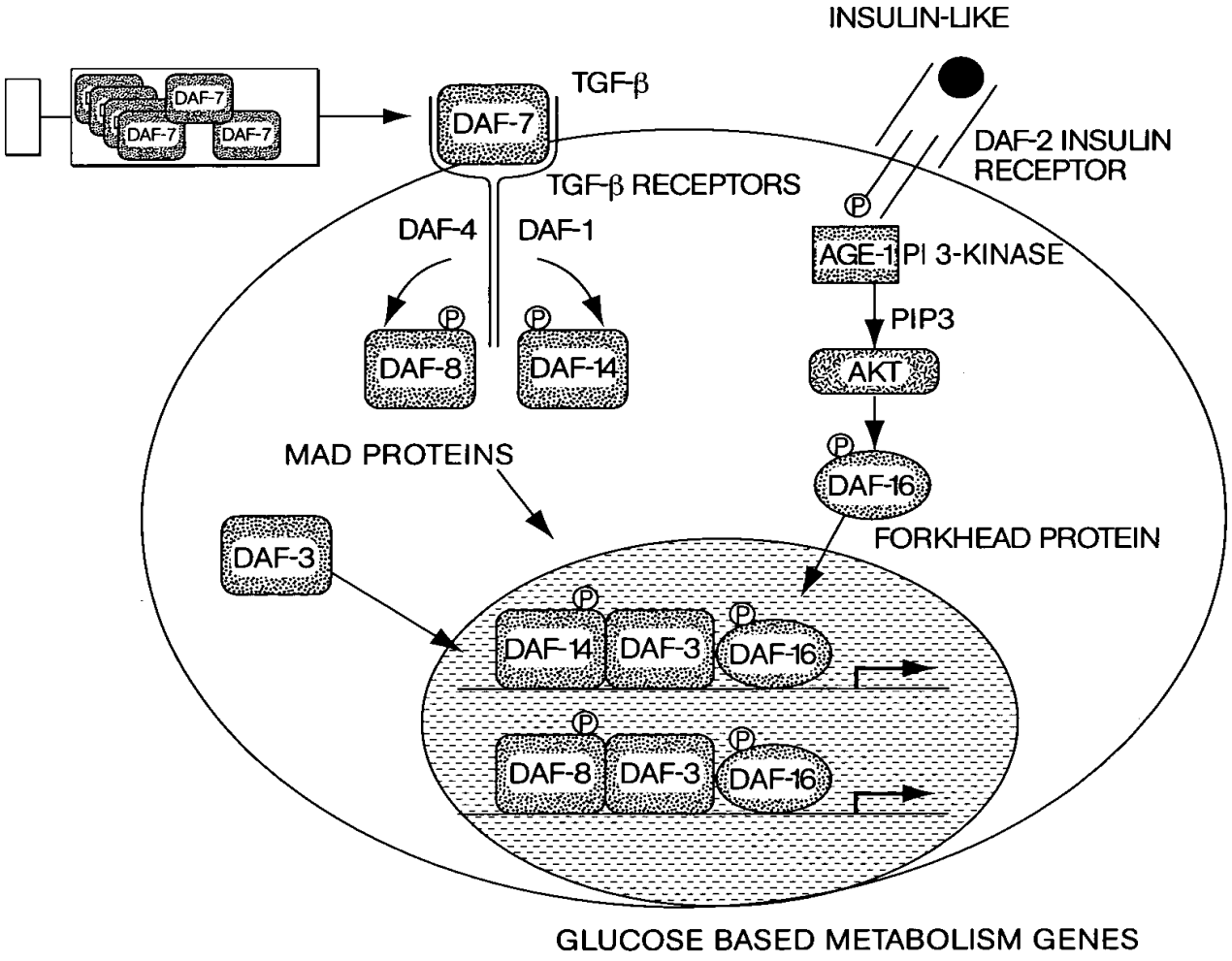


Fig. 23

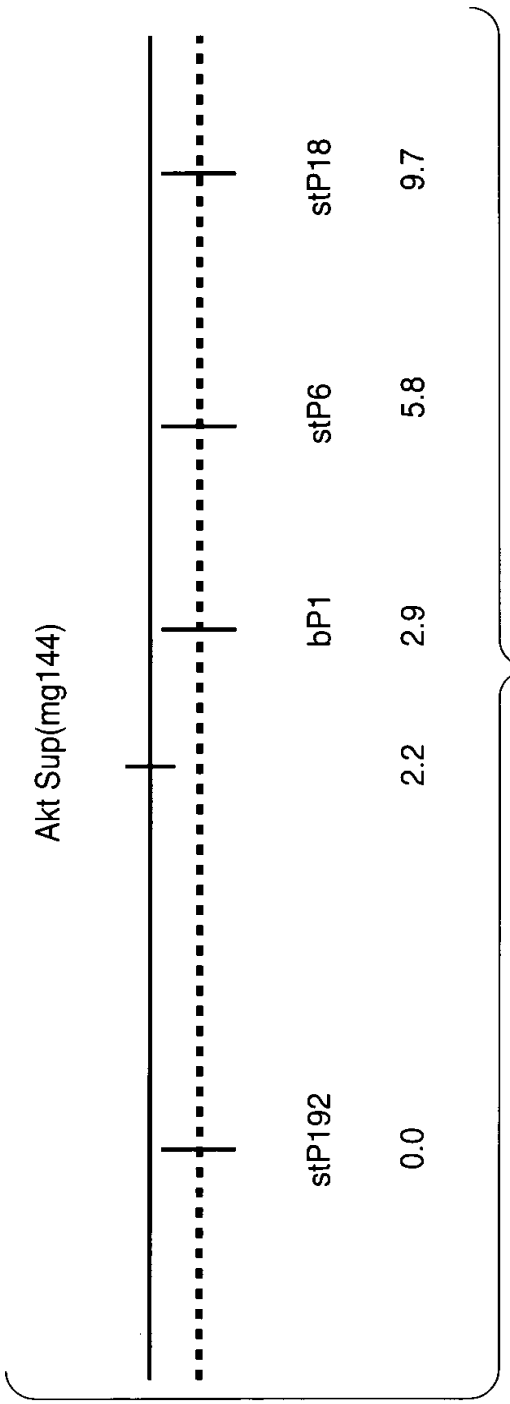


Fig. 24

Comparison of the human AKT protein sequence to the cosmid sequence C12D8, located in the genetic interval where sup(mg144) maps. Numbering in the AKT protein sequence by amino acid residues, and in the cosmid sequence by nucleotide position.

```
 Score = 450 (207.4 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
 Identities = 79/121 (65%), Positives = 97/121 (80%), Frame = +1

Query:    319 EVLEDNDYGRAVDWWGLGVVMYEMMCGRLPFYNQDHEKLFELILMEEIRFPRTLGPEAKS 378
              +VL+D+DYGR VDWWG+GVVMYEMMCGRLPFY++DH KLFELI+  ++RFP  L  EA++
Sbjct:  33685 QVLDDHDYGRCVDWWGVGVVMYEMMCGRLPFYSKDHNKLFELIMAGDLRFPSKLSQEART 33864

Query:    379 LLSGLLKKDPTQRLGGGSEDAKEIMQHRFFANIVWQDVYEKKLSPPFKPQVTSETDTRYFD 439
              LL+GLL KDPTQRLGGG EDA EI +  FF  + W+  Y K++ PP+KP V SETDT YFD
Sbjct:  33865 LLTGLLVKDPTQRLGGGPEDALEICRADFFRTVDWEATYRKEIEPPYKPNVQSETDTSYFD 34047

 Score = 256 (118.0 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
 Identities = 48/66 (72%), Positives = 59/66 (89%), Frame = +1

Query:    146 TMNEFEYLKLLGKGTFGKVILVKEKATGRYYAMKILKKEVIVAKDEVAHTLTENRVLQNS 205
              TM +F++LK+LGKGTFGKVIL KEK T + YA+KILKK+VI+A++EVAHTLTENRVLQ
Sbjct:  32314 TMEDFDFLKVLGKGTFGKVILCKEKRTQKLYAIKILKKDVIIAREEVAHTLTENRVLQRC 32493

Query:    206 RHPFLT 211
              +HPFLT
Sbjct:  32494 KHPFLT 32511

 Score = 190 (87.6 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
 Identities = 36/45 (80%), Positives = 37/45 (82%), Frame = +2

Query:    276 KLENLMLDKDGHIKITDFGLCKEGIKDGATMKTFCGTPEYLAPEV 320
              KLENL+LDKDGHIKI DFGLCKE I  G    TFCGTPEYLAPEV
Sbjct:  33509 KLENLLLDKDGHIKIADFGLCKEEISFGDKTSTFCGTPEYLAPEV 33643

 Score = 188 (86.7 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
 Identities = 37/57 (64%), Positives = 42/57 (73%), Frame = +3

Query:    209 FLTALKYSFQTHDRLCFVMEYANGGELFFHLSRERVFSEDRARFYGAEIVSALDYLH 265
              +   LKYSFQ    LCFVM++ANGGELF H+ +   FSE RARFYGAEIV AL YLH
Sbjct:  32667 YFQELKYSFQEQHYLCFVMQFANGGELFTHVRKCGTFSEPRARFYGAEIVLALGYLH 32837

 Score = 166 (76.5 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
 Identities = 29/59 (49%), Positives = 42/59 (71%), Frame = +1

Query:     53 NNFSVAQCQLMKTERPRPNTFIIRCLQWTTVIERTFHVETPEEREEWATAIQTVADGLK 111
              + F++   Q M  E+PRPN F++RCLQWTTVIERTF+ E+ E R+ W  AI++++   K
Sbjct:  31846 STFAIFYFQTMLFEKPRPNMFMVRCLQWTTVIERTFYAESAEVRQRWIHAIESISKKYK 32022

 Score = 134 (61.8 bits), Expect = 5.2e-167, Sum P(8) = 5.2e-167
 Identities = 24/33 (72%), Positives = 30/33 (90%), Frame = +3

Query:    210 LTALKYSFQTHDRLCFVMEYANGGELFFHLSRE 242
              L  LKYSFQT+DRLCFVME+A GG+L++HL+RE
Sbjct:  33156 LQELKYSFQTNDRLCFVMEFAIGGDLYYHLNRE 33254
```

Fig. 25

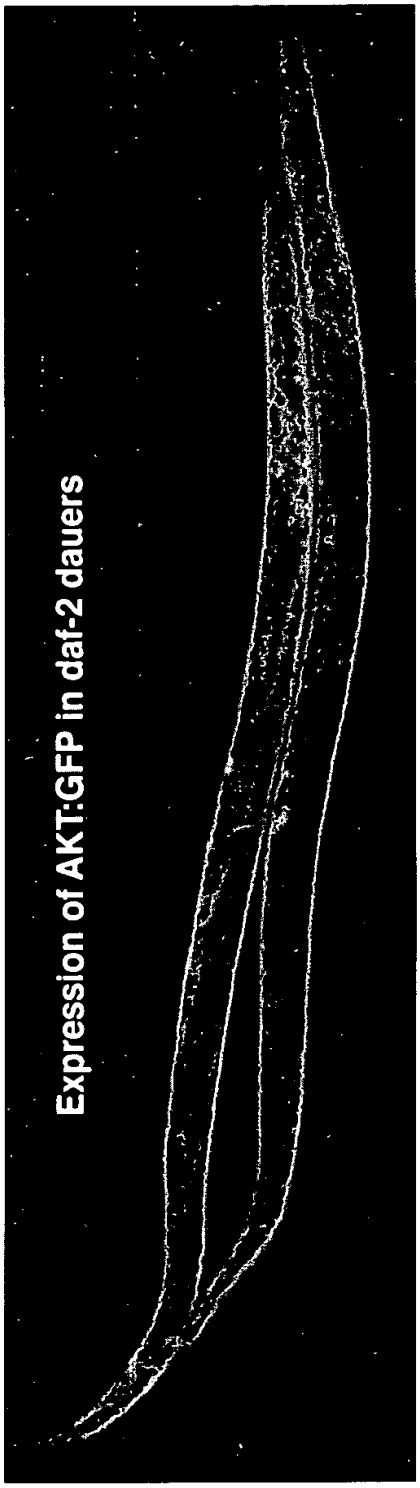


Fig. 26A

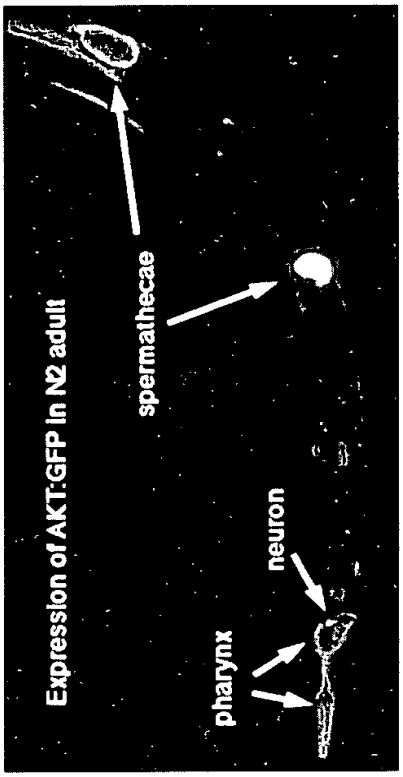
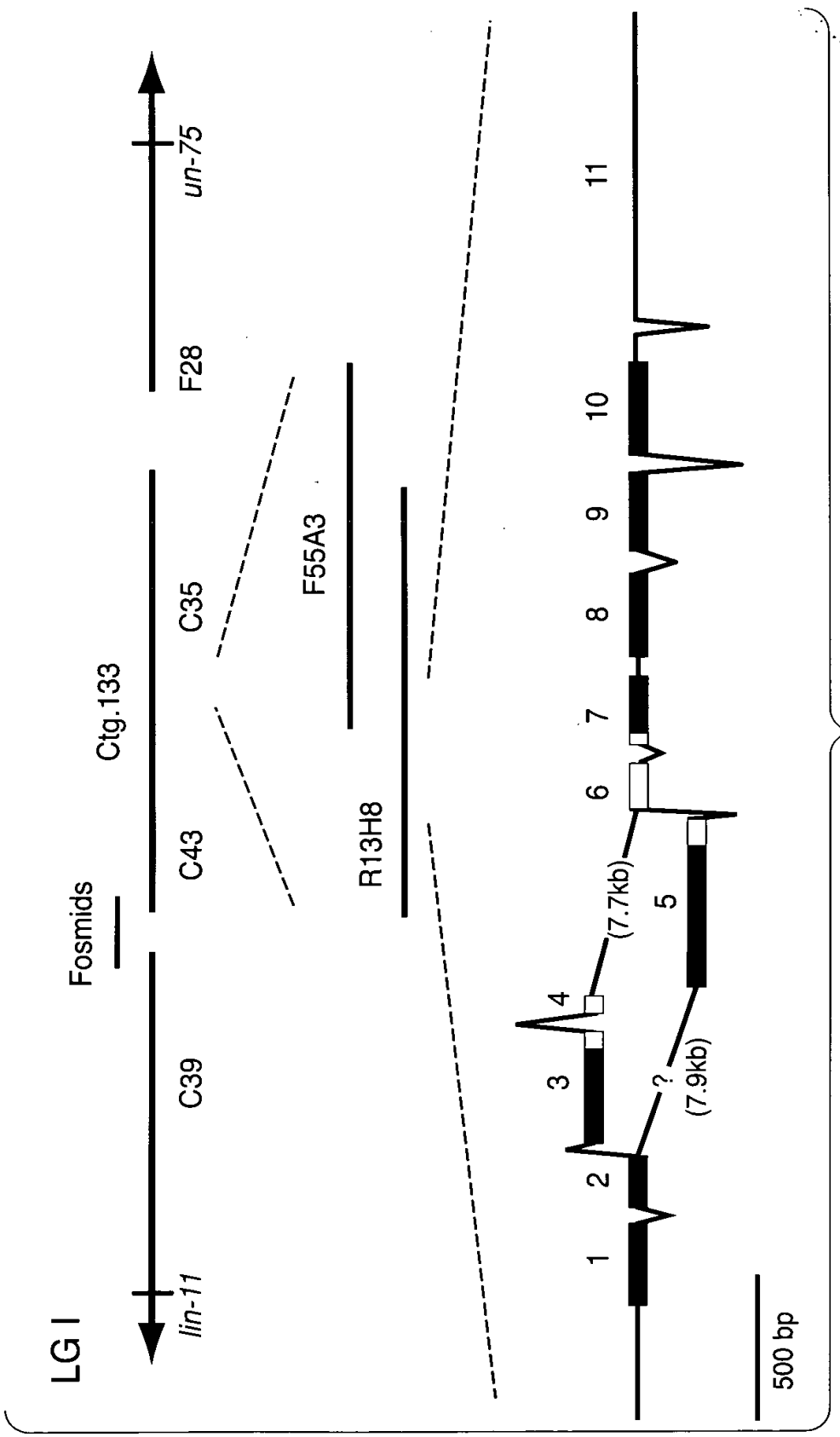


Fig. 26B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lin-11
C39
Fosmids
C43
Ctg.133
C35
F28
un-75
F55A3
R13H8
1
2
3
4
5
6
7
8
9
10
11
(7.7kb)
?
(7.9kb)
500 bp

Fig. 27

```
           1               15 16              30 31              45 46              60
1 ZK84.6   -MNSVFTIIFVLCAL QVAASFRQSFG---P SMSEESASMQLLREL QH--NMMESAHRPMP  54
2 ZK75.1   -MFSFFT-YFLLSAL LLSASCRQ------P SMDT-SKADRILREI E----METELENQLS  47
3 ZK1251.2 ----MPPIILVFFLV LIPASQQY------P FSLE-SLNDQIINEE VI--EYMLENSIRSS  47
4 C06E2    --MIVTLIVFLVIGL QMAHLSQVSGNNENG FLNP-FDLSQWSEEI LHRQYHHHHHHHHGN  57
5 ZK75.2   ----MNAIIFCLLFT TVTATYEVF-----G KGIEHRNEHLIINQL D---IIPVESTPTPN  48
6 ZK75.3   MKLSVVLALFIIFQL GAASLMRN------W MFDFEKELEHDYDDS E---IGFHNIHSLMA  51
7 C17C3    --------------- --------------- ---------MKLLHI F---IIFLLFQSCSN  18
8 F13B12   --------------- --------------- ----MYWFRQVYRPS FF--FGFLAILLLSS  50
9 INSULIN  --------------- --------------- ------------MA LWMRLLPLLALLALW  17
CONSENSUS  --------------- --------------- --------------- ---------------

           61              75 76              90 91             105 106             120
1 ZK84.6   RARRVPAPGETRACG RKLISLVMAVCGD-L CN-------------- ---------------  85
2 ZK75.1   RARRVPA-GEVRACG RRLLLFVWSTCGE-P CT-------------- ---------------  77
3 ZK1251.2 RTRRVPDEKKIYRCG RRIHSYVFAVCGK-A CE-------------- ---------------  78
4 C06E2    RARRTLETEKIYRCG RKLYTDVLSACNG-P CE-------------- ---------------  88
5 ZK75.2   RASRVQK----RLCG RRLILFMLATCG--E CD-------------- ---------------  74
6 ZK75.3   RSRRGDK---VKICG TKVLKMVMVMCGG-E CS-------------- ---------------  79
7 C17C3    KMCQYSK-KKYKICG VRALKHMKVYCTR-G MT-------------- ---------------  48
8 F13B12    PTPSDAS---IRLCG SRLTTTLLAVCRNQL CTGLTAFKRSADQSY APTTRDLFHIHHQQ-  80
9 INSULIN  GPDPAAAFVNQHLCG SHLVEALYLVCGERG FFYTPKTRREAEDLQ VGQVELGGGPGAGSL   77
CONSENSUS  --------------CG -----------C---- ---------------- ---------------
                          B CHAIN                          C PEPTIDE

           121             135 136             150 151             165 166             180
1 ZK84.6   -------PQEGKDIA TECCGNQCSDDYIRS ACCP-----    112
2 ZK75.1   -------PQEDMDIA TVCCTTQCTPSYIKQ ACCPEK---    106
3 ZK1251.2 -------SNTEVNIA SKCCREECTDDFIRK QCCP-----    105
4 C06E2    -------PGTEQDLS KLCCGNQCTFVEIRK ACCADKL--    118
5 ZK75.2   -------TDSSEDLS HICCIKQCDVQDIIR VCCPNSFRK    106
6 ZK75.3   -------S-TNENIA TECCEKMCTMEDITT KCCPSR---    107
7 C17C3    -------R-DYGKLL VTCCSKGCNAIDIQR ICL------     73
8 F13B12   ---------KRGGIA TECCEKRCSFAYLKT FCCNQDDN-    109
9 INSULIN  QPLALEGSLQKRGIV EQCCTSICSLYQLEN YCN-------    110
CONSENSUS  ------------------CC---C------- --C-------
                          A CHAIN
```

Fig. 28

```
Zk75-1             ACGRRLLLFV WSTCGEPCTx xxQEDMDIAT VCCTTQCTPS YIKQAC46
Zk84-6             Acgrklislv mavcgdlcnx xxqegkdiat ecccgnqcsdd yirsac46
Zk1251-2           RCGRRIHSYV FAVCGKACEx xxSTEVNIAS KCCREECTDD FIRKQC46
C06e2              RCGRKLYTDV LSACNGPCEx xxGTEQDLSK LCCGNQCTFV EIRKAC46
Zk75-3             ICGTKVLKMV MVMCGGECSx xxSTNENIAT ECCEKMCTME DITTKC46
Zk75-2             lcgrrlilfm latcgecdtx xxDSSEDLSH ICCIKqcdvq diirvc46
Ins-Human          LCGSHLVEAL YLVCGERGFx xxLQKRGIVE QCCTSICSLY QLENYC46
Ins-Rabbit         lcgshlveal ylvcgergfx xxtpksgive qcctsicsly qlenyc46
Ins1-Xenopus       lcgshlveal ylvcgdrgfx xxkmkrgive qcchstcslf qlesyc46
Ins2-Xenopus       lcgshlveal ylvcgdrgfx xxkmkrgive qcchstcslf qlenyc46
Ins-Alligator      lcgshlvdal ylvcgergfx xxspkggive qcchntcsly qlenyc46
Ins-Elephantfish   lcgshlvdal yfvcgergfx xxpkqigive qcchntcslv nlegyc46
Igf1-Bovine        LCGAELVDAL QFVCGDRGFx xxAPQTGIVD ECCFRSCDLR RLEMYC46
Igf1-Dog           lcgaelvdal qfvcgdrgfx xxapqtgivd eccfrscdlr rlemyc46
Igf2-Horse         lcggelvdtl qfvcgdrgfx xxrrsrgive eccfrscdla llletyc46
Igf2-Human         LCGGELVDTL QFVCGDRGFx xxRRSRGIVE ECCFRSCDLA LLETYC46
Ilp-Amphioxus      LCGSTLADVL SFVCGNRGYx xxRRRRGLVE ECCYNVCDYS QLESYC46
Lirp-Locust        YCGEKLSNAL KLVCRGNYNx xxRRTRGVFD ECCRKSCSIS ELQTYC46
Bxa4-Bommo         YCGRHLARTL ADLCWEAGVx xxRGKRGIVD ECCLRPCSVD VLLSYC46
Bxb1-Bommo         YCGRHLADTL ADICFGVEKx xxRGKRGVVD ECCFRPCTLD VLLSYC46
Bxrpa-Hornworm     icgrhlartl adlcpnveyx xxgkragvad dccvnsctmd vllsyc46
Bxa1-Silkworm      ycgrrlatml sfvcdnqyqx xxgkrqgiae eccnkpcten ellgyc46
Bxa2-Silkworm      YCGRRLATML LYVCDNQYQx xxGKRQGIVE ECCNKPCTEN ELLGYC46
Bax3-Silkworm      ycgrrlaiml sylcdnqylx xxgkrqgiae eccnkpcted ellgyc46
F13b12             LCGSRLTTTL LAVCRNQLCx xxQKRGGIAT ECCEKRCSFA YLKTFC46
Mpi3-Seasnail      LCGSTLANMV QWLCSTYTTx xxESRPSIVC ECCFNQCTVQ ELLAYC46
Relaxin-Human      LCGRELVRAQ IAICGMSTWx xxRPYVALFE KCCLIGCTKR SLAKYC46
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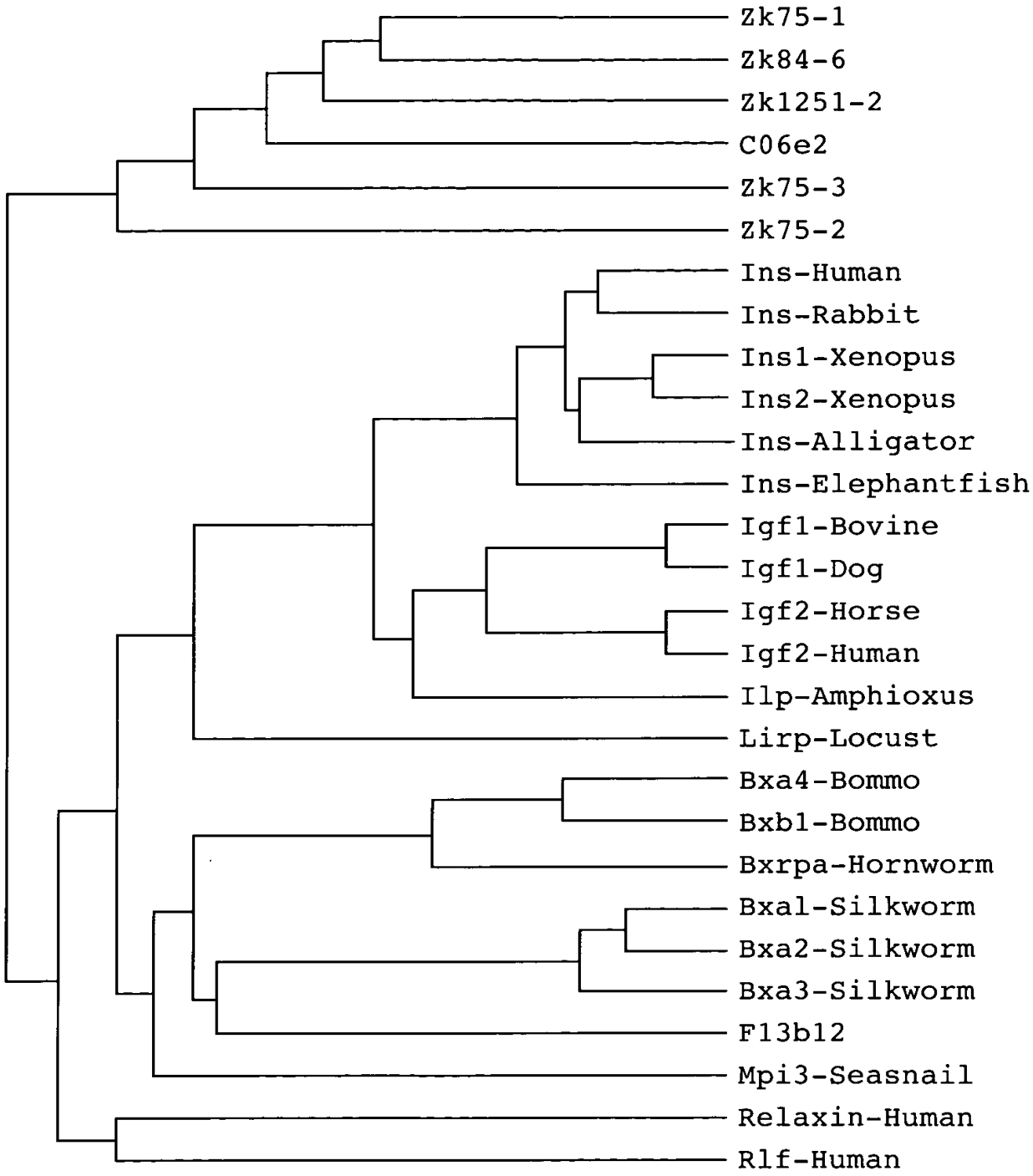
Fig. 29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Ins2-Xenopus
Ins-Alligator
Ins-Elephantfish
Igf1-Bovine
Igf1-Dog
Igf2-Horse
Igf2-Human
Ilp-Amphioxus
Lirp-Locust
Bxa4-Bommo
Bxb1-Bommo
Bxrpa-Hornworm
Bxa1-Silkworm
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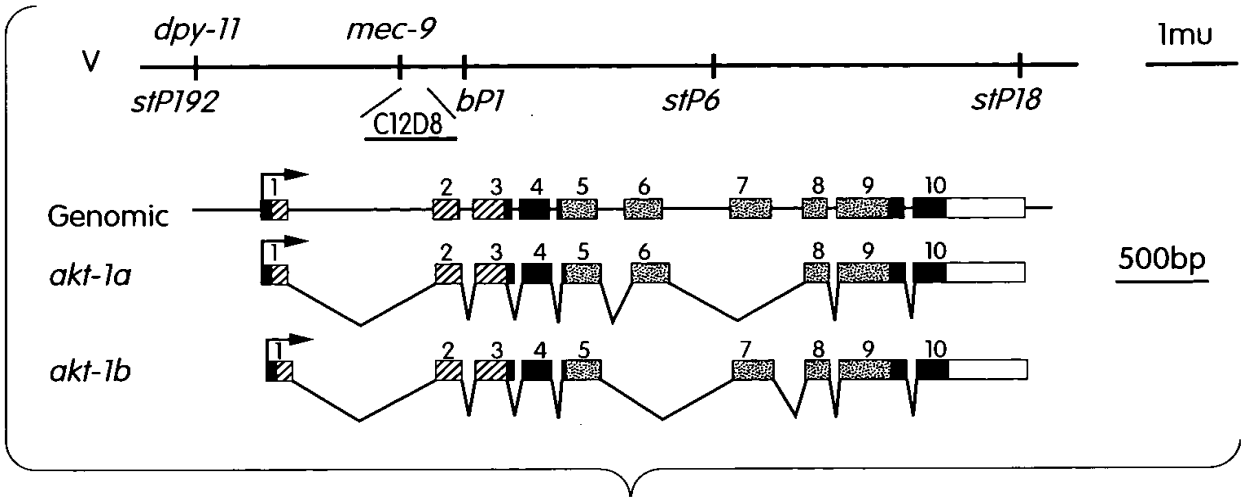
Mpi3-Seasnail
Relaxin-Human
Rlf-Human

Fig. 30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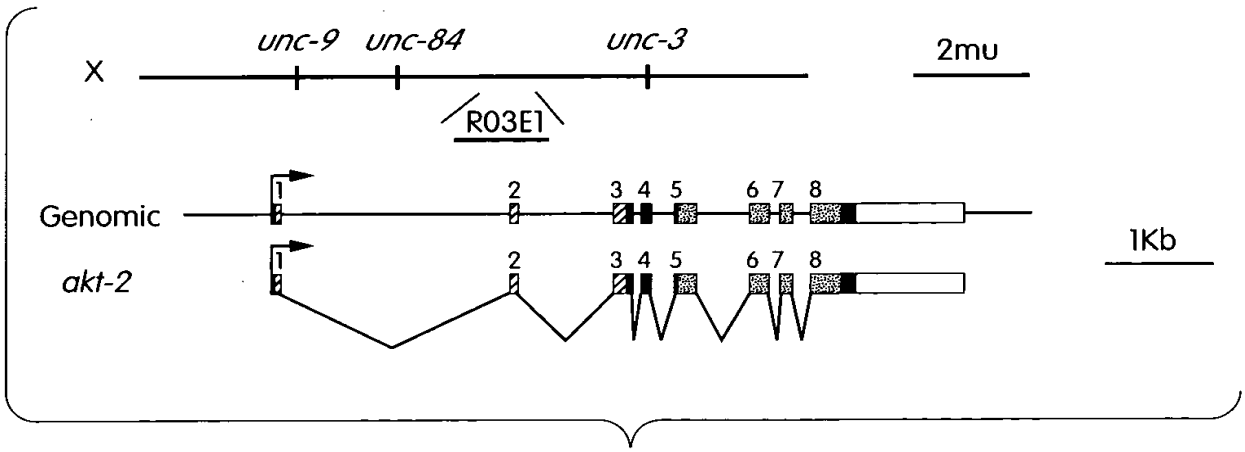
akt-1b
500bp

Fig. 31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Genomic
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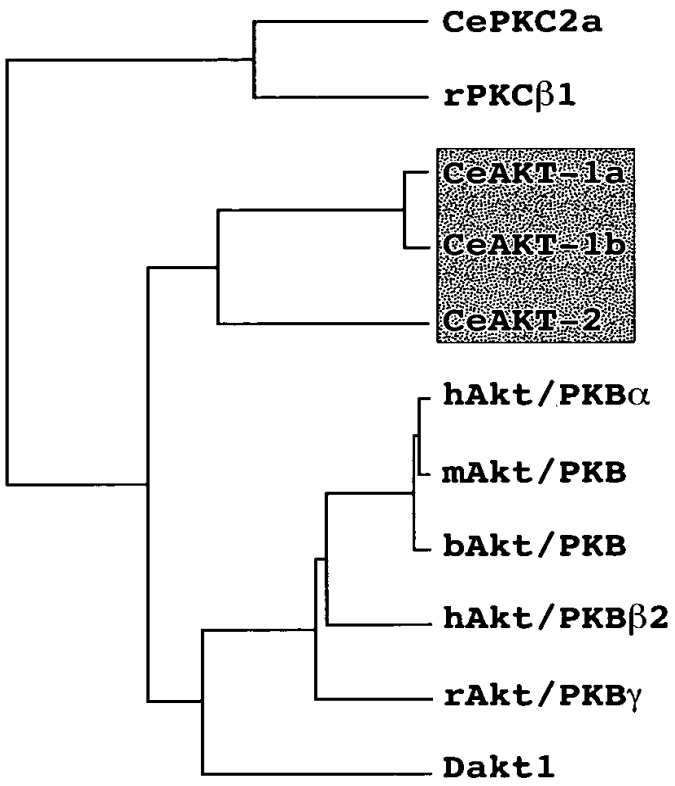
Fig. 32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rPKCβ1
CeAKT-1a
CeAKT-1b
CeAKT-2
hAkt/PKBα
mAkt/PKB
bAkt/PKB
hAkt/PKBβ2
rAkt/PKBγ
Dakt1

Fig. 33

```
AKT-1a      MSMTSLSTKSRR--QEDVVIEGWLHKKGEHIRNWRPRYFMIFNDGALLGFRAKPKEGQPFPEPL
AKT-1b      ............--...............................................
AKT-2            M..ENAHLQK..I..S.....................IL.R.T...S...D.L....
hAkt/PKBa              MSDVAI.K.....R..Y.KT.....LLK...TFI.YKER.QDVDQREA...

AKT-1a      NDFMIKDAATMLFEKPRPNMFMVRCLQWTTVIERTFYAESAEVRQRWIHAIESIS--KKYKGTN
AKT-1b      ...........................................................--.....
AKT-2       .N...R....VCLD.....I.....................D..DF.....E..QAV.SHNRL.ENA
hAkt/PKBa   .N.SVAQCQL.KT.R...T.II..............HV.TP.E.EE.TT..QTVADGL.KQE--
                                                                  mg144 T
AKT-1a      ANPQEELMETNQQPKIDEDSEFAGAAHAIMGQPSSGHGDNCSIDFRASMISIADTSEAAKRDKI
AKT-1b      ............................................................
AKT-2       G.TSMQEED..GN.SGES.VNM---------DAT.TRS..---..ESTVMN.DEPE.VPRKNTV
hAkt/PKBa   ----------------E.EMD.----------R.GSPS..SGAE-------EMEV.L.KPKHRV

AKT-1a      TMEDFDFLKVLGKGTFGKVILCKEKRTQKLYAIKILKKDVIIAREEVAHTLTENRVLQRCKHPF
AKT-1b      ............................................................
AKT-2       ..D.........Q.......R..SSD.....IR.EMVVD.S.............YA.V...
hAkt/PKBa   ..NE.EY..L.............V...A.GRY..M.....E..V.KD.............NSR...

AKT-1a      LTELKYSFQEQHYLCFVMQFANGGELFTHVRK----CGTFSEPRARFYGAEIVLALGYLH-RC
AKT-1b      .........TNDR....E..I..D.YY.LNREVQMNKEG.........S.........-AN
AKT-2       ..L.....A.YHI....E.........LQR-----K...A.T...S..I.......-HR
hAkt/PKBa     A.....THDR....EY.......F.LSRE----RV...D.........S..D...SEK
                                                  •
AKT-1a      DIVYRDMKLENLLLDKDGHIKIADFGLCKEEISFGDKTSTFCGTPEYLAPEVLDDHDYGRCVDW
AKT-1b      S.....L.....................................................
AKT-2       N.............R.....T.........KY.....................IE.I..D.S...
hAkt/PKBa   NV....L.....M.........T.......G.KD.ATMK.................E.N....A...

AKT-1a      WGVGVVMYEMMCGRLPFYSKDHNKLFELIMAGDLRFPSKLSQEARTLLTGLLVKDPTQRLGGGP
AKT-1b      ............................................................
AKT-2       ..................SA.ENG.....TTC..K..NR..P..V...S...ERV.AK...A...
hAkt/PKBa     .L..............NQ..E.....LMEEI...RT.GP..KS..S...K...K.....S
AKT-1a      EDALEICRADFFRTVDWEATYRKEIEPPYKPNVQSETDTSYFDN-EFTSQPVQLTPPSRSGALA
AKT-1b      ..........-.................................-..................
AKT-2       D..R.VS..E..KD......L...V...F....M......F..RVRYV.ILLKV-----.E.I
hAkt/PKBa     ...K...MQHR..AGIV.QHV.E.KLS..F..Q.T.....R...E-...A.MITI...DQDDSME
                  •
AKT-1a      TVDEQEEMQSNFTQFSFHNVMGSINRIHEASEDNEDYDMGZ
AKT-1b      ..........................................
AKT-2
hAkt/PKBa   C..--S.RRPH.P...YSASSTA
```

Fig. 34

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Fig. 35A

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TTTCAATGCAAATGGACAAGAAGTCGCCTTGAAGGCTCACCTCCCTTCTACTCCCCACAAAATCACCATCAAACAAATCACACTTTTGTATCATT
TTGCGTCC

Fig. 35B

MEDLTPTNTSLDTTTTNNDTTSDREAAPTTLNLTPTASESENSLSPVTAEDLIAKSIKEGCPKRTSNDFMFLQSMGEG
AYSQVFRCREVATDAMFAVKVLQKSYLNRHQKMDAIIREKNILTYLSQECGGHPFVTQLYTHFHDQARIYFVIGLV
ENGDLGESLCHFGSFDMLTSKFFASEILTGLQFLHDNKIVHRDMKPDNVLIQKDGHILITDFGSAQAFGGLQLSQEGFT
DANQASSRSSDSGSPPPTRFYSDEEEENTARRTTFVGTALYVSPEMLADGDVGPQTDIWGLGCILFQCLAGQPPFRAV
NQYHLLKRIQELDFSFPEGFPEEASEIIAKILVRDPSTRITSQELMAHKFFENVDWVNIANIKPPVLHAYIPATFGEP
EYYSNIGPVEPGLDDRALFRLMNLGNDASASQPSTPSNVEHRGDPFVSEIAPRANSEAEKNRAARAQKLEEQRVK
NPFHIFTNNSLILKQGYLEKKRGLFARRRMFLLTEGPHLLYIDVPNLVLKGEVPWTPCMQVELKNSGTFFIHTPNR
VYYLFDLEKKADEWCKAINDVRKRYSVTIEKTFNSAMRDGTFGSIYGKKKSRKEMMREQKALRRKQEKEEKKAL
KAEQVSKKLSMQMDKKSP

Fig. 36

MEDLTPTNTSLDTTTTNNDTTSDREAAPTTLNLTPTASESENSLSPVTAEDLIAKSIKEGCPKRTSNDFMFLQSMGEG
AYSQVFRCREVATDAMFAVKVLQKSYLNRHQKMDAIIREKNILTYLSQECGGHPFVTQLYTHFHDQARIYFVIGLV
ENGDLGESLCHFGSFDMLTSKFFASEILTGLQFLHDNKIVHRDMKPDNVLIQKDGHILITDFGSAQAFGGLQLSQEGFT
DANQASSRSSDSGSPPPTRFYSDEEVPEENTARRTTFVGTALYVSPEMLADGDVGPQTDIWGLGCILFQCLAGQPPFR
AVNQYHLLKRIQELDFSFPEGFPEEASEIIAKILVRDPSTRITSQELMAHKFFENVDWVNIANIKPPVLHAYIPATF
GEPEYYSNIGPVEPGLDDRALFRLMNLGNDASASQPSTFRPSNVEHRGDPFVSEIAPRANSEAEKNRAARAQKLEE
QRVKNPFHIFTNNSLILKQGYLEKKRGLFARRRMFLLTEGPHLLYIDVPNLVLKGEVPWTPCMQVELKNSGTFFIH
TPNRVYYLFDLEKKADEWCKAINDVRKRYSVTIEKTFNSAMRDGTFGSIYGKKKSRKEMMREQKALRRKQEKEE
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Fig. 37

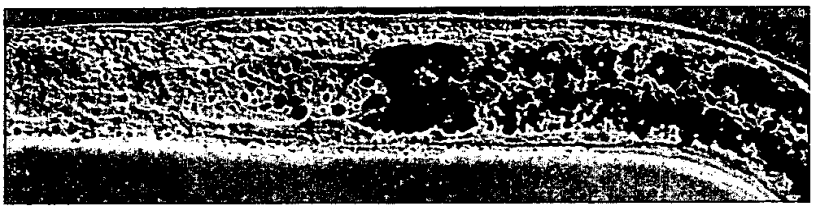

Fig. 38A

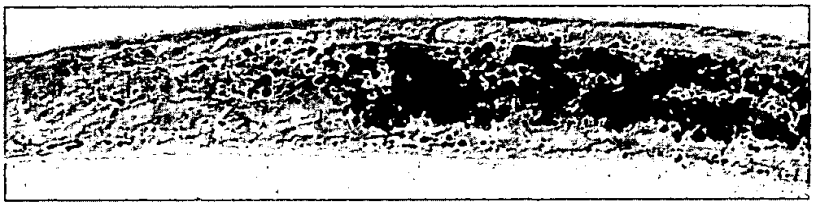

Fig. 38B

Fig. 38C

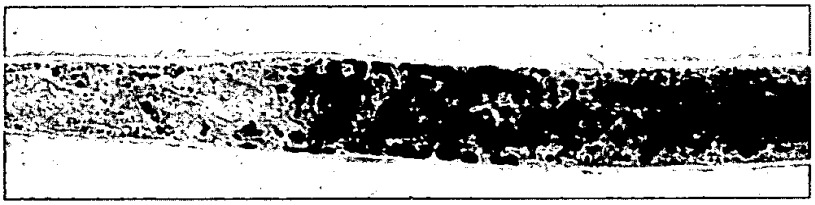

Fig. 38D

Fig. 38E

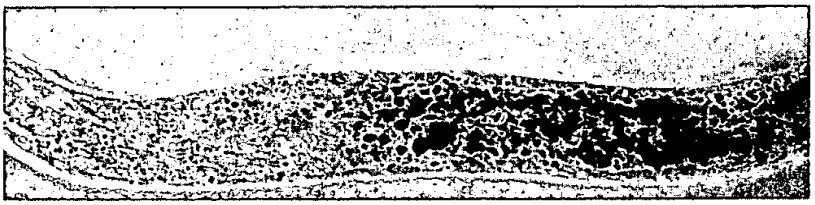

Fig. 38F

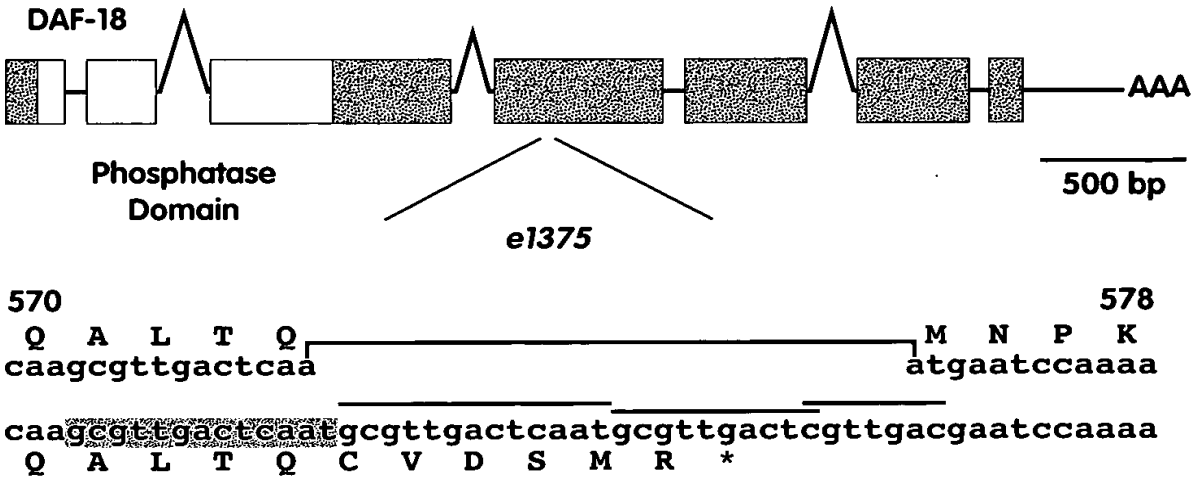

Fig. 39A

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DAF-18   48 IFRTAVSSNR CRTEYQNIDL DCAYITDRII AIGYPAIGIE ANFRNSKVQT
PTEN      4 IIKEIVSRNK RRYQEDGFDL DLTYIYPNII AMGFPAERLE GVYRNNIDDV

DAF-18   98 QQFLTRRHGK GNVKVFNLRG GYYYDADNFD GNVICFDMTD HHPPSLELMA
PTEN     54 VRFLDSKH.K NHYKIYNLCA ERHYDTAKFN CRVAQYPFED HNPPQLELIK

DAF-18  148 PFCREAKEWL EADDKHVIAV HCKAGKGRTG VMICALLIYI NFYPSPRQIL
PTEN    103 PFCEDLDQWL SEDDNHVAAI HCKAGKGRTG VMICAYLLHR GKFLKAQEAL

DAF-18  198 DYYSIIRTKN NKGVTIPSQR RYIYYYHKLR ERELNYLPLR MQLIGVYVER
PTEN    153 DFYGEVRTRD KKGVTIPSQR RYVYYYSYLL KNHLDYRPVA LLFHKMMFET

DAF-18  248 PPKTWGGGSK IKVEVGNGST ILFKPD..PL IISKSNHQRE RATWLNNCDT
PTEN    203 IPMFSGGTCN PQFVVCQLKV KIYSSNSGPT RREDKFMYFE FPQPLPVCGD
```

Fig. 39B

DAF-18 Protein

MVTPPPDVPSTSTRSMARDLQENPNRQPGEPRVSEPYHNSIVERIRHIFRTAVSSNRCRTEYQNIDLDCAYITDRIIAIG
YPATGIEANFRNSKVQTQQFLTRRHGKGNVKVFNLRGGYYYDADNFDGNVICFDMTDHHPPSLELMAPFCREAKEWLEAD
DKHVIAVHCKAGKGRTGVMICALLIYINFYPSPRQILDYYSIIRTKNNKGVTIPSQRRYIYYYHKLRERELNYLPLRMQL
IGVYVERPPKTWGGGSKIKVEVGNGSTILFKPDPLIISKSNHQRERATWLNNCDTPNEFDTGEQKYHGFVSKRAYCFMVP
EDAPVFVEGDVRIDIREIGFLKKFSDGKIGHVWFNTMFACDGGLNGGHFEYVDKTQPYIGDDTSIGRKNGMRRNETPMRK
IDPETGNEFESPWQIVNPPGLEKHITEEQAMENYTNYGMIPPRYTISKILHEKHEKGIVKDDYNDRKLPMGDKSYTESGK
SGDIRGVGGPFEIPYKAEEHVLTFPVYEMDRALKSKDLNNGMKLHVVLRCVDTRDSKMMEKSEVFGNLAFHNESTRRLQA
LTQMNPKWRPEPCAFGSKGAEMHYPPSVRYSSNDGKYNGACSENLVSDFFEHRNIAVLNRYCRYFYKQRSTSRSRYPRKF
RYCPLIKKHFYIPADTDDVDENGQPFFHSPEHYIKEQEKIDAEKAAKGIENTGPSTSGSSAPGTIKKTEASQSDKVKPAT
EDELPPARLPDNVRRFPVVGVDFENPEEESCEHKTVESIAGFEPLEHLFHESYHPNTAGNMLRQDYHTDSEVKIAEQEAK
AFVDQLLNGQGVLQEFMKQFKVPSDNSFADYVTGQAEVFKAQIALLEQSEDFQRVQANAEEVDLEHTLGEAFERFGHVVE
ESNGSSKNPKALKTREQMVKETGKDTQKTRNHVLLHLEANHRVQIERRETCPELHPEDKIPRIAHFSENSFSDSNFDQAI
YL

Fig. 40A

```
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  61 gaccaggtcg atggctcgtg accttcaaga gaatccaaac cgacaacctg gtgaaccacg
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 181 tgtatcttcc aatcgttgtc gcaccgagta ccaaaatatc gacctagatt gtgcatatat
 241 cacagaccga atcatagcta tcggttatcc agcaacagga atcgaagcga atttccgtaa
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 661 aattccatca caacgacgct acatttacta ctaccataag cttcgtgaac gtgagctcaa
 721 ctatttacca ttgagaatgc agttgattgg tgtctacgtg gaacggcctc caaagacatg
 781 gggtggtggt tcaaagataa aagtggaggt tggaaatggc tcgacaattt tatttaagcc
 841 ggatcctctc ataatctcca aatcaaatca tcagcgagag cgtgcgacgt ggctgaacaa
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1261 gtggcaaata gtgaatcctc ctggactgga aaaacatatt acggaggaac aagcaatgga
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1381 aaagcatgaa aaaggtatcg tcaaggatga ctataatgat cgtaagctgc caatgggaga
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1561 attgaagagt aaagatctta acaacggaat gaaacttcac gttgttcttc gttgtgtaga
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1681 tgaatcgaca cggaggcttc aagcgttgac tcaaatgaat ccaaaatggc gacctgaacc
1741 gtgtgcgttc ggatccaaag gtgctgaaat gcattaccct ccgtcggttc gatattcaag
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1861 cagaaatatt gccgttctta atcgatattg ccgatatttc tacaagcaac gcagtacatc
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2341 ataccatcca aatacggccg gtaacatgct gcgtcaggat tatcacactg attcggaagt
2401 gaaaatagct gaacaagagg caaaagcctt cgttgaccag ttgcttaatg gacaaggtgt
2461 attacaagag tttatgaagc aattcaaagt accatcggac aattcctttg ctgattatgt
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Fig. 40B (sheet 1 of 2)

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2641 tgagcgattc gggcacgttg tagaagaatc gaatggttct tctaaaaatc caaaagccct
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3301 ataa
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Fig. 40B (sheet 2 of 2)

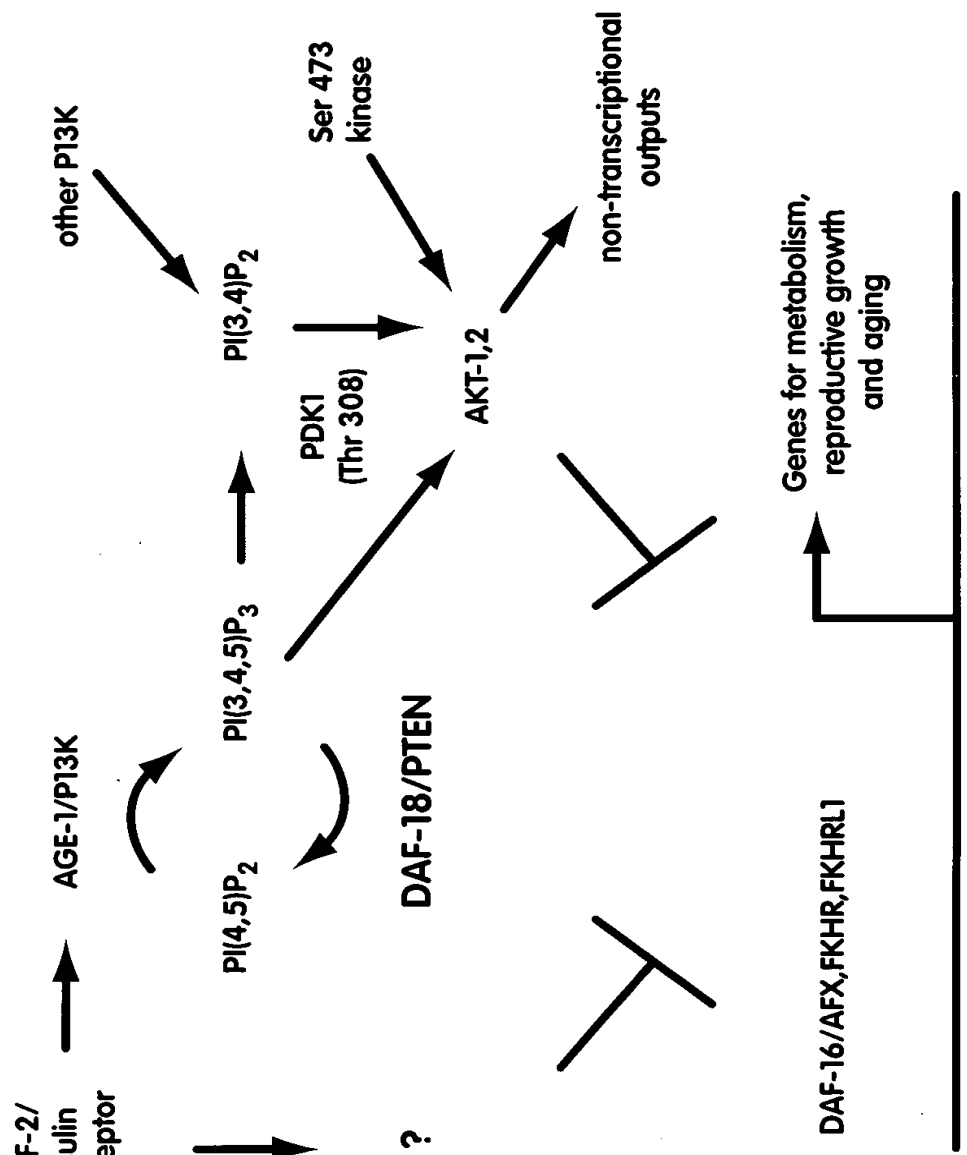

Fig. 41

```
                                                                                               ttta
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M   K   F   Q   Y   Y   S   K   K   A   A   G   K   T   M   S   N   S   V   S

atg tcc agt gac aat cgc atg gag gat ttt aaa cgt cgt ttt cgt cga agt gga tcg tta
M   S   S   D   N   R   M   E   D   F   K   R   R   F   R   R   S   G   S   L

gga att cca ttt gtc cca gaa gaa gat gtt aaa caa ctc ttc aca cca act cgt act gtt
G   I   P   F   V   P   E   E   D   V   K   Q   L   F   T   P   T   R   T   V

cgt cga gaa gca tst att cgc gaa ggg gat gag gaa gaa gga gta caa att ctc aca ata
R   R   E   A   S   I   R   E   G   D   E   E   E   G   V   R   I   L   T   I

att gtc aag tca agt cgt gtt tcg gag gat atc tca aaa atg att gca aac ctc cct gat
I   V   K   S   S   R   V   S   E   D   I   S   K   M   I   A   N   L   P   D

cac act cgt atc aaa cat ttg gag act cgt gac agt caa gat gga agt tcc aaa act atg
H   T   R   I   K   H   L   E   T   R   D   S   Q   D   G   S   S   K   T   M

gat gtt ctt cta gag att gag ctc ttt cat tat gga aaa caa gaa gca atg gat ctt atg
D   V   L   L   E   I   E   L   F   H   Y   G   K   Q   E   A   M   D   L   M

aga ctt aat ggg ctt gat gtt cat gag gtg tca tcg act att cgt cca act gca ata aaa
R   L   N   G   L   D   V   H   E   V   S   S   T   I   R   P   T   A   I   K

gag caa tat aca gag cct gga tct gat gat gcg aca acc ggt tct gaa tgg ttt cca aaa
E   Q   Y   T   E   P   G   S   D   D   A   T   T   G   S   E   W   F   P   K

agt att tat gat ttg gat att tgt gca aaa aga gtg att atg tat gga gca ggg ctg gac
S   I   Y   D   L   D   I   C   A   K   R   V   I   M   Y   G   A   G   L   D

gct gat cat cct ggt ttc aaa gat acc gag tat cgt caa cgt cga atg atg ttt gct gaa
A   D   H   P   G   F   K   D   T   E   Y   R   Q   R   R   M   M   F   A   E

ctg gcg ctc aat tac aaa cac ggt gag cca att ccg cga acc gaa tat aca tca tcc gaa
L   A   L   N   Y   K   H   G   E   P   I   P   R   T   E   Y   T   S   S   E

cgg aaa act tgg gga att ata tat aga aaa ttg aga gaa ttg cac aaa aag cac gca tgc
R   K   T   W   G   I   I   Y   R   K   L   R   E   L   H   K   K   H   A   C
```

Fig. 42 (sheet 1 of 2)

```
aag cag ttt ctt gat aac ttt gag cta ctg gag aga cat tgt gga tac tcg gaa aat aat
K   Q   F   L   D   N   F   E   L   L   E   R   H   C   G   Y   S   E   N   N

att ccg caa cta gaa gat atc tgc aag ttt ttg aaa gca aaa act gga ttc cgt gtt cgc
I   P   Q   L   E   D   I   C   K   F   L   K   A   K   T   G   F   R   V   R

cca gtc gcc gga tac tta tca gct cgt gat ttc ttg gca ggt ctt gca tat cgt gtc ttc
P   V   A   G   Y   L   S   A   R   D   F   L   A   G   L   A   Y   R   V   F

ttc tgc act caa tac gtt cgc cat cat gcc gat cca ttt tac act cca gaa cca gac acc
F   C   T   Q   Y   V   R   H   H   A   D   P   F   Y   T   P   E   P   D   T

gtt cac gag ctc atg ggt cac atg gct cta ttc gct gat cca gat ttt gct cag ttt tct
V   H   E   L   M   G   H   M   A   L   F   A   D   P   D   F   A   Q   F   S

caa gag att gga tta gct tct ctt gga gca tca gag gaa gat ttg aag aag ctt gca aca
Q   E   I   G   L   A   S   L   G   A   S   E   E   D   L   K   K   L   A   T

ctc tac ttc ttt tcc att gaa ttt ggt ctc tcg tct gat gac gct gcc gat tct cca gta
L   Y   F   F   S   I   E   F   G   L   S   S   D   D   A   A   D   S   P   V

aaa gaa aat gga tca aat cat gaa aga ttt aaa gta tac gga gca gga ctt ctg agc agt
K   E   N   G   S   N   H   E   R   F   K   V   Y   G   A   G   L   L   S   S

gct ggc gag ttg caa cat gcc gtt gag ggt agt gca acc att att cgt ttt gat ccg gat
A   G   E   L   Q   H   A   V   E   G   S   A   T   I   I   R   F   D   P   D

cgt gtt gtt gag caa gaa tgt ctc att act act ttc cag tca gcg tat ttc tat act aga
R   V   V   E   Q   E   C   L   I   T   T   F   Q   S   A   Y   F   Y   T   R

aat ttt gaa gag gcc cag cag aaa ctc aga atg ttc acc aac aac atg aaa cgt ccc ttc
N   F   E   E   A   Q   Q   K   L   R   M   F   T   N   N   M   K   R   P   F

att gtt cgt tac aac cca tac aca gaa agc gtc gaa gtt ctc aac aac tcc cgt tcc att
I   V   R   Y   N   P   Y   T   E   S   V   E   V   L   N   N   S   R   S   I

atg ttg gca gtg aac tct ctc cgc tca gac atc aac ctg ctc gcc gga gct ctc cac tac
M   L   A   V   N   S   L   R   S   D   I   N   L   L   A   G   A   L   H   Y

atc ctg tag
I   L   *
```

Fig. 42 (sheet 2 of 2)

```
                                                  attacccaagtttgaggtagcattgctctcttcaatcat
atg gat tcg ttg ttt cag atg gca tcc gca atg aag ttt caa tac tac tcg aag aaa gct
M   D   S   L   F   Q   M   A   S   A   M   K   F   Q   Y   Y   S   K   K   A

gct gga aag aca atg tct aat agt gtc aaa aac tgg att ccg tgt tcg ccc agt cgc cgg
A   G   K   T   M   S   N   S   V   K   N   W   I   P   C   S   P   S   R   R

ata ctt atc agc tcg tga ttt ctt ggc agg tct tgc ata tcg tgt ctt ctt ctg cac tca
I   L   I   S   S   *

ata cgt tcg cca tca tgc cga tcc att tta cac tcc aga acc aga cac cgt tca cga gct
cat ggg·tca cat ggc tct att cgc tga tcc aga ttt tgc tca gtt ttc tca aga gat tgg
att agc ttc tct tgg agc atc aga gga aga ttt gaa gaa gct tgc aac act cta ctt ctt
ttc cat tga att tgg tct ctc gtc tga tga cgc tgc cga ttc tcc agt aaa aga aaa tgg
atc aaa tca tga aag att taa agt ata cgg agc agg act tct gag cag tgc tgg cga gtt
gca aca tgc cgt tga ggg tag tgc aac cat tat tcg ttt tga tcc gga tcg tgt tgt tga
gca aga atg tct cat tac tac ttt cca gtc agc gta ttt cta tac tag aaa ttt tga aga
ggc cca gca gaa act cag aat gtt cac caa caa cat gaa acg tcc ctt cat tgt tcg tta
caa ccc ata cac aga aag cgt cga agt tct caa caa ctc ccg ttc cat tat gtt ggc agt
gaa ctc tct ccg ctc aga cat caa cct gct cgc cgg agc tct cca cta cat cct gta g
```

Fig. 43

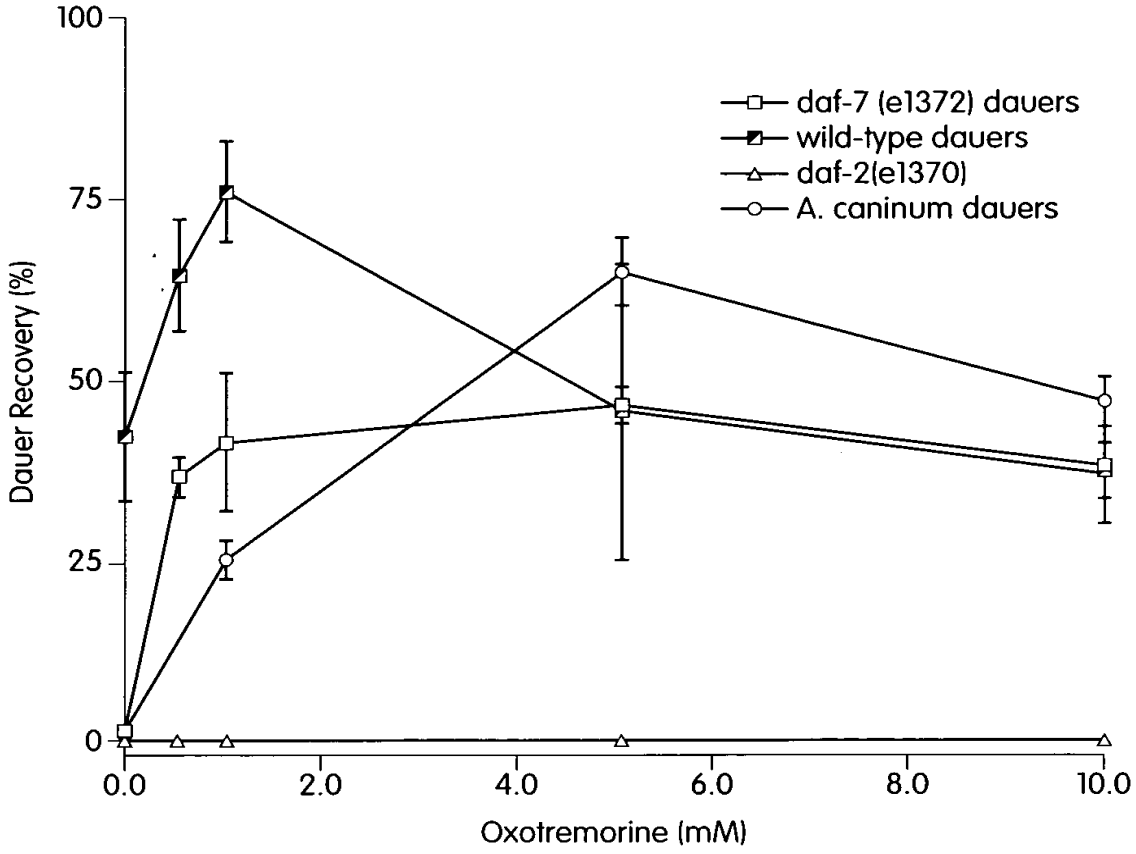
100
75
50
25
0
Dauer Recovery (%)
0.0
2.0
4.0
6.0
8.0
10.0
Oxotremorine (mM)
daf-7 (e1372) dauers
wild-type dauers
daf-2(e1370)
A. caninum dauers

Fig. 44A

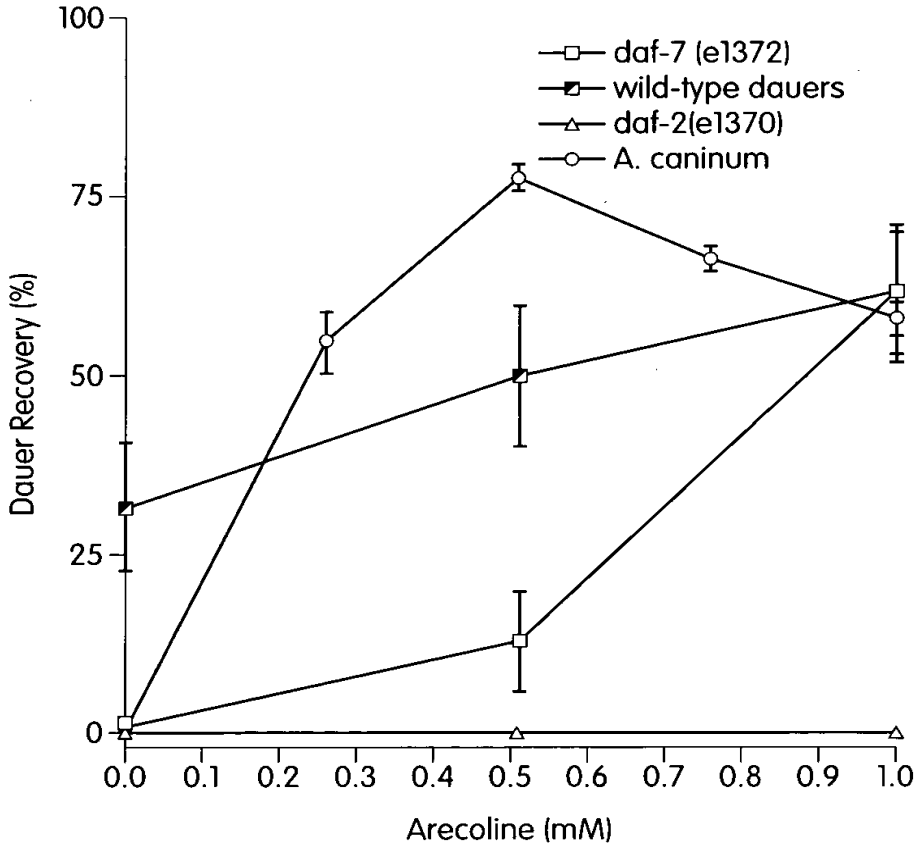
daf-7 (e1372)
wild-type dauers
daf-2(e1370)
A. caninum
Dauer Recovery (%)
100
75
50
25
0
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
Arecoline (mM)

Fig. 44B

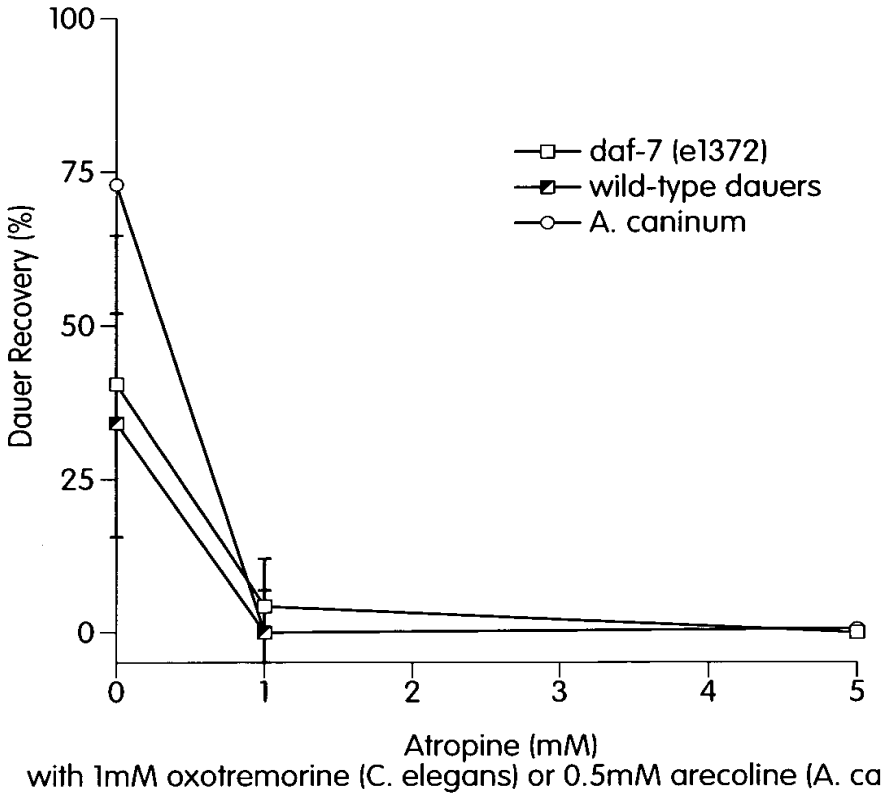
100
75
50
25
0
Dauer Recovery (%)
daf-7 (e1372)
wild-type dauers
A. caninum
0
1
2
3
4
5
Atropine (mM)
with 1mM oxotremorine (C. elegans) or 0.5mM arecoline (A. caninum)

Fig. 44C

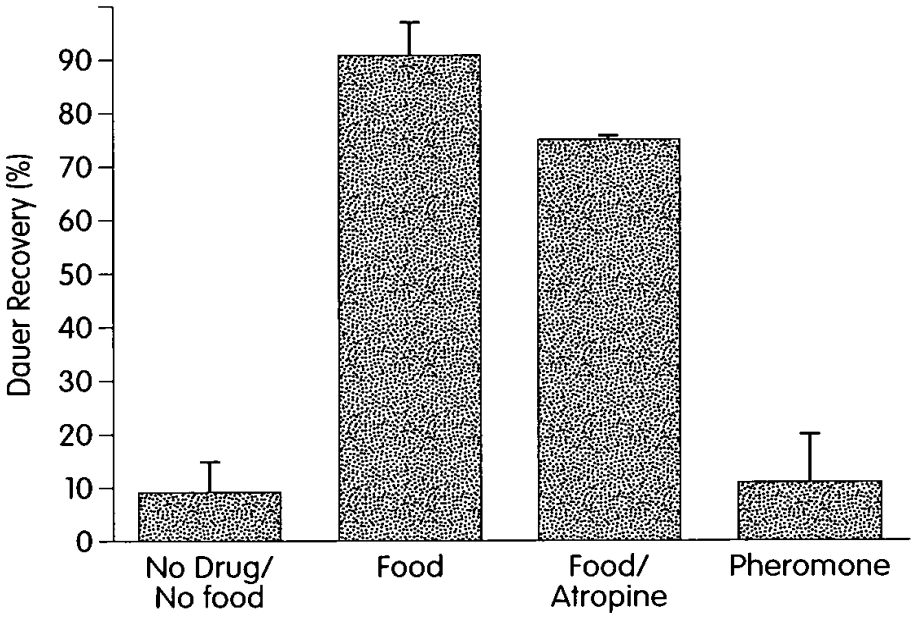
Dauer Recovery (%)
90
80
70
60
50
40
30
20
10
0
No Drug/
No food
Food
Food/
Atropine
Pheromone

Fig. 45A

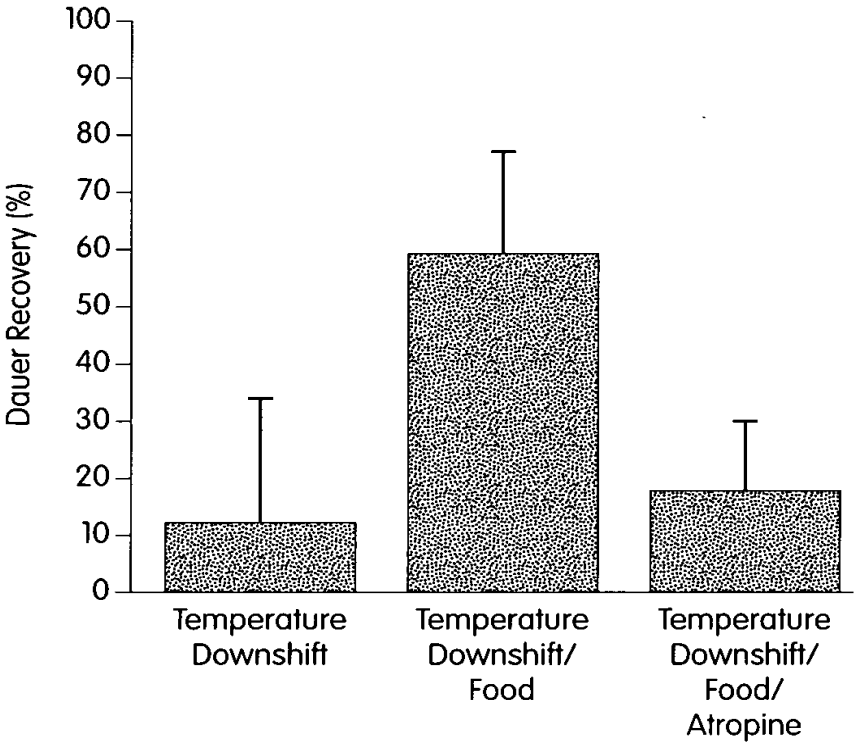
Dauer Recovery (%)
100
90
80
70
60
50
40
30
20
10
0
Temperature Downshift
Temperature Downshift/ Food
Temperature Downshift/ Food/ Atropine

Fig. 45B

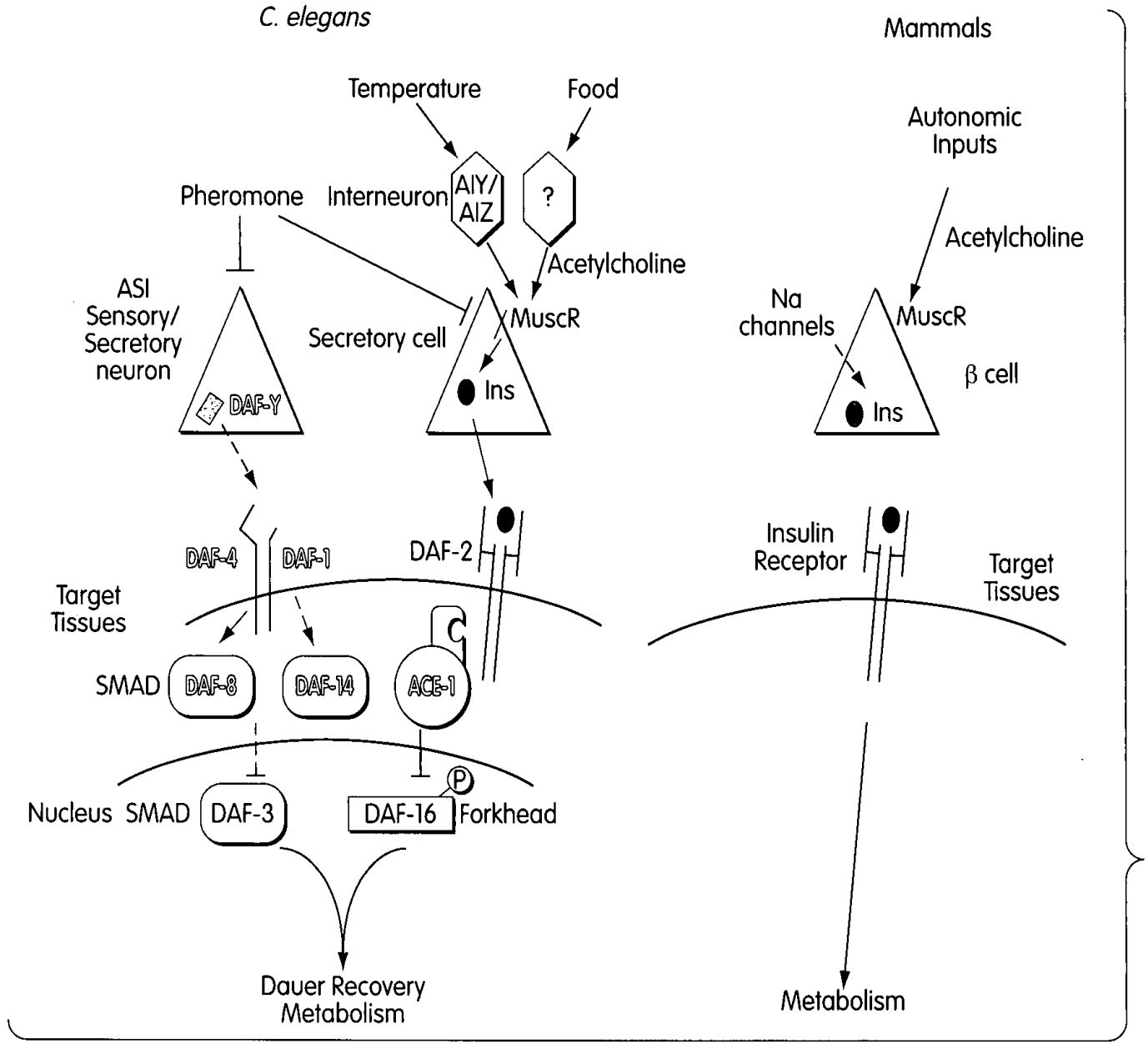
C. elegans
Mammals
Temperature
Food
Pheromone
Interneuron
AIY/
AIZ
?
Acetylcholine
ASI
Sensory/
Secretory
neuron
DAF-Y
Secretory cell
MuscR
Ins
Autonomic
Inputs
Acetylcholine
Na
channels
MuscR
β cell
Ins
DAF-4
DAF-1
DAF-2
Target
Tissues
Insulin
Receptor
Target
Tissues
C
SMAD
DAF-8
DAF-14
ACE-1
Nucleus SMAD
DAF-3
P
DAF-16
Forkhead
Dauer Recovery
Metabolism
Metabolism

Fig. 46

```
ATTCGGCATGAGCATGGaGCTTCGAGTCCTAGAGAACACAAAACGTTCCCGGCGGAACCTGGGtCTGGACTGCGAC
GAGACTCAAGCGAGTCCCGCTGCTGCCGATATCCCCTCACAGTGGACTTTGAGGCTTTCGGCTGGGACTGGATCAT
CGCACCTAAGCGCTACAAGGCCAACTACTGCTCCGGCCAGTGGGAGTACATGTTCATGCAAAAATATCCGCATACC
CATTTGGTGCAGCAGGCCAATCCAAGAGGTTATGcTGGGCCCTGTTGTACCCCCACCAAGATGTCCCCAATcAACA
TgcTctACTTCAATGACAAGCAGCAGATTATcTACGGCAAGATCCCTGGCATGGTGGTGGATCGCTGTGGcTGCTC
TTAAGGTGGGGGATAGAGGATGCCTCCCCCACAGACCGTACCCCAAGACCCATAGCCcTGCCCAATCCACCGCCTG
ATCCAAACAT
```

Fig. 47A

```
IRHEHGASSPREHKTFPAEPGSGLRRDSSESRCCRYPLTVDFEAFGWDWIIAPKRYKANYCSGQWEYMFMQKYPHT
HLVQQANPRGYAGPCCTPTKMSPINMLYFNDKQQIIYGKIPLAMVVDRCGCS
```

Fig. 47B